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METHODS FOR IMPROVING OPERABILITY IN THE AGED*

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During the past thirty years, the mortality rate following major operations has been reduced by more than 50 per cent. A predominant factor in this reduction appears to have been preoperative improvement in nutrition, although better anesthesia, blood replacement, and the correction of dehydration and electrolyte imbalances have also contributed.

Malnutrition is found consistently in geriatric patients with malignant disease and other serious disorders. In 1953, while giving the Sixth Annual Roswell Park Lecture sponsored by the Buffalo Surgical Society, one of us (W. H. C.) pointed out that only recently had it been realized that aged patients would tolerate major operations almost as well as younger people, provided decrements were corrected beforehand.

Using data from the Illinois Research and Educational Hospital, an institution with no private beds, two groups of patients undergoing operation were compared (1). In the group undergoing radical mastectomy, cholecystectomy, colectomy, gastrectomy, herniorrhaphy or thyroidectomy, there was no significant difference in hospital mortality rates between patients who had reached the age of 60 and those who were younger. In the second group, whose operations included colostomy, esophagectomy, radical surgery of the head and neck, pneumonectomy or abdominoperineal resection, the hospital mortality rate was more than twice as great in patients past the age of 60 than in patients who were younger.

Probably the greatest initial difference between these groups was in the need for thorough preoperative correction of associated disease states and improvement in nutrition. Barring emergency situations, everything is to be gained and nothing lost by approximately one week of intensive preoperative evaluation and preparation.

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IMPROVEMENT OF OPERABILITY

Six important factors

For the past six or seven years, we have stressed the importance of the following 6 factors besides nutrition:

1. Blood count and blood volume. The elderly patient is frequently admitted to the hospital in a dehydrated state that causes initial hemograms to be misleading. Therefore, hydration is accomplished immediately upon admission, and blood counts are repeated when hydration is thought to have reached its maximum. If weight loss, particularly recent weight loss, has been significant, blood volume studies usually are performed. When blood volume is deficient, aggressive replacement of blood is started immediately.

It is far more effective to restore blood volume to normal several days prior to surgery than to try to make up the deficiency at the time of operation. Accomplished early, the appetite and physical activity of the patient will generally improve noticeably.

2. Cardiac reserve. The patient's tolerance for exercise and his cardiac symptoms are determined by the history. A preoperative electrocardiogram is essential in case postoperative problems occur, and especially in order to rule out the presence of a recent myocardial infarct, even though on occasion such infarcts are asymptomatic. In 1952, de Peyster, Paul and Gilchrist (2) dramatically demonstrated that myocardial infarcts occurring less than three months prior to surgery contraindicate all except the most heroic surgical procedures. The only cardiac abnormalities that would seriously contraindicate surgery are: 1) active heart failure, 2) complete heart block, and 3) recent myocardial infarction. The first two can be corrected preoperatively, but only time can correct the last.

3. Renal status. In elderly males (because of possible prostatic obstruction) and females, renal status must be evaluated by either blood nonprotein nitrogen or urea nitrogen studies, or both. Any renal damage that exists should be corrected prior to major surgery. In a male with prostatic obstruction, this may be temporarily accomplished by drainage with a Foley catheter pending the completion of urgent surgery. The prostatic condition can then be corrected as a secondary procedure, if necessary. In an elderly patient, the relief of obstruction or infection will usually improve the renal status promptly.

4. Serum proteins. The determination of serum protein concentration and the albumin-globulin ratio is mandatory, since these values indicate not only the general nutritional state of the patient, but also the capacity for healing. Blood plasma, protein hydrolysates and supplementary diets, if used aggressively, can improve the protein status rapidly.

5. Avoidance of preoperative bed rest. The importance of avoiding preoperative bed rest in preparation for surgery is frequently overlooked. Every effort should be made to mobilize the patient preoperatively. Muscle tone will determine his ability to cough, to move, and be active postoperatively. Good muscle tone will decrease the incidence of atelectasis and of thrombophlebitis—two of the most important and most frequent complications of surgery in the aged.

6. Liver function. Important in the determination of liver function in the aged are the thymol turbidity, cephalin flocculation and bromsulfalein tests (the

latter the most valuable single test, provided jaundice is not present), particularly when abdominal disease exists. Unless irreparable damage to the liver is present, function can be improved by a strenuous nutritional regimen.

Nutrition

Although none of the foregoing factors is secondary in importance, the major emphasis of this presentation is on nutrition in the preoperative period. In the malnourished patient, not only is there a decreased reserve with impaired response to stress, but frequently a negative nitrogen balance. Operative mortality and morbidity can be reduced greatly, if weight loss can be stopped and the nutritional curve started upward. Since the majority of malnourished patients on the Surgical Service of Illinois Research and Educational Hospital are cancer victims, time is important. Therefore, a maximum of one week of aggressive effort to improve nutrition is allowed. This enhances greatly the patient's tolerance of surgery without jeopardizing cancer therapy.

To order a high protein and high caloric diet is not sufficient. Most of these patients have anorexia, and no matter what food is placed before them, they will not eat. All too frequently, a patient given a diet of 3000 to 3500 calories will be found to consume at the most 500 to 1000 calories. To overcome this deficiency, we have established an intensive nutritional regimen consisting of an oral intake up to the level of the patient's maximum ability, parenteral injection of protein hydrolysates, tube feedings administered during the night (if they do not seriously impair the patient's appetite), and the intravenous administration of fat emulsions. Although not of caloric value, the improvement in serum protein concentration accomplished by administration of plasma and the rapid correction of hypovolemia achieved by the administration of blood, combine with better nutrition to produce an upswing in the weight curve. Our objective is a weight gain of 4 to 5 pounds within the five to seven days allowed for this regimen.

ACTH therapy. Reports previously have been made on the value of adrenocorticotropin (ACTH) in improving operability. ACTH improves appetite and brings about euphoria and a general sense of well-being. It also frequently has an anti-inflammatory effect. As a result, patients may eat ravenously within hours after the onset of its action, and also rapidly progress from a bedridden to an ambulatory state. Part of the initial weight gain represents water retention due to steroid therapy. Nevertheless, the sharp increase in food intake improves the patient's nutrition and operability. A few illustrative cases follow:

A 55-year-old woman was admitted with a pelvic abscess secondary to perforation of carcinoma of the rectum. Her temperature rose daily to 102°F. She was mentally depressed, almost totally anoretic, and bedridden. Chemotherapy failed to reduce her fever. A colostomy was performed without benefit. Three weeks thereafter, an attempt was made to resect the tumor, but it was abandoned because of severe tachycardia. The patient's condition continued to deteriorate. ACTH therapy was then started, in a dosage of 25 mg. four times daily. Within twenty-four hours she was cheerful, had a ravenous appetite, and became ambulatory. She had not been out of bed, to our knowledge, for three to four weeks before this time. The temperature dropped promptly and remained at a reasonable level, and there was a progressive weight gain. Five days later, a successful abdominoperineal resection was performed.

A 60-year-old malnourished woman with chronic cholecystitis, had a history of severe anorexia and nausea. ACTH was administered for six days preoperatively. During this period, the patient consumed 2500 to 3000 calories daily. Her weight rose from 115 to 122 pounds, and she was able to tolerate surgery well.

A 64-year-old man with what proved to be a nonresectable carcinoma of the head of the pancreas, was jaundiced. It was almost impossible to persuade him to eat. Upon the administration of 80 units of ACTH daily, his weight rose from 137 to 143 pounds in five days and he tolerated surgery well, although the tumor could not be resected.

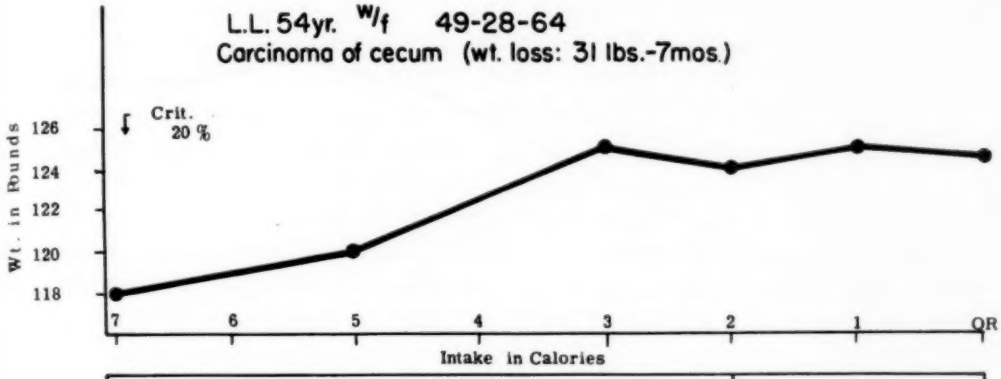
Postoperatively, a sharp weight reduction occurred in each of these patients. This was due in part to the diuresis of retained water. Some postoperative weight loss was to be expected when intake was minimal or nil. Nevertheless, conversion to a positive nitrogen balance for a short time prior to surgery is an important adjunctive measure.

Fat emulsion. The newest nutritional supplement is the fat emulsion, Lipomul-I.V. When it first became commercially available in 1958, it was an emulsion of 15 per cent cottonseed oil with soybean phosphatides as emulsifiers and Pluronic-F-68 as a stabilizer in a vehicle of 4 per cent dextrose in water. Six hundred cubic centimeters of Lipomul-I.V. furnished 900 calories.

A colleague, Dr. William Marshall (3), analyzed the results of administering a total of 580 units (a unit = 600 cc.) of this emulsion in a series of 95 patients. Some patients had minor reactions, the most frequent of which was an elevation in systolic blood pressure of slightly more than 10 mm. of Hg. A few patients had mild episodes of hypotension. Nonspecific nausea and vomiting, subjective symptoms of weakness, and a rash occurred in one patient. Several pyrogenic reactions occurred. Prior to commercial distribution, pyrogenic reactions were a major factor in delaying the introduction of intravenous fat emulsion. Dr. Marshall concluded from this and other studies that the parenteral administration of fat emulsion was sufficiently free of severe reactions to permit its unrestricted clinical use. We believe, however, that a margin of safety should be maintained by limiting the quantity to 1800 calories (2 units) daily for a maximum of nine successive days. Recently, the manufacturer (Upjohn) improved this fat emulsion by substituting cocoanut oil for cottonseed oil.

Tube feeding. Another step in our intensive nutritional preparation is nightly tube feeding. A small polyethylene feeding tube is passed into the stomach through the nose and kept in place throughout the preparatory period. The small tube is well tolerated for long periods of time. The tube feeding contains 350 calories in each 500 cc. More concentrated tube feedings can be prepared, but their high fat content causes diarrhea. Diarrhea occurs occasionally with the formula that we use, so it is frequently necessary to add tincture of paregoric. The tube feeding is administered by slow continuous drip throughout the night, completing it two to three hours before breakfast, so that the stomach will not be full at breakfast time and cause anorexia.

Protein hydrolysates. Although protein hydrolysates such as Amigen or Aminosol supply only 400 calories per liter, they are of value when basic caloric requirements are met by other means. If the basic caloric requirements are not furnished by other means, protein hydrolysates are converted to glycogen and utilized as such rather than being synthesized to urgently needed proteins.



Oral	2500					2000	
Tube	350						
Amigen		400					
Lipomul IV.		900		1800		900	
Total Calories	2850	4150		5050		3650	2750
Blood		500 cc.	500 cc.	1000 cc	1000 cc.	500 cc	

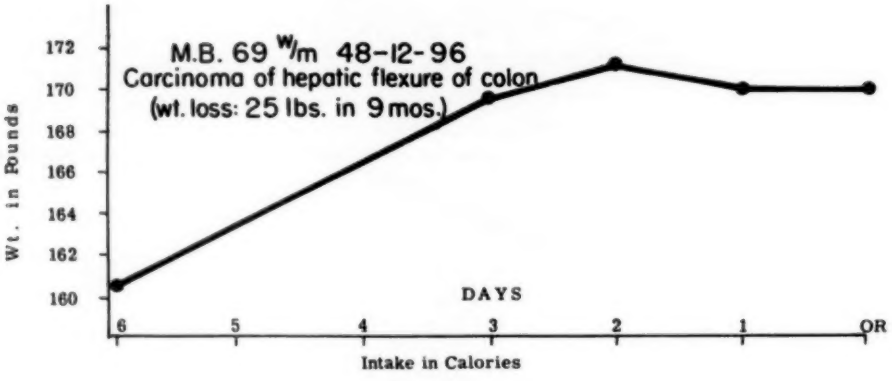
FIG. 1. Seven-day presurgical preparation of a debilitated patient by administration of nutritional supplements and whole blood.

General. Use of this scheme of intensive nutritional therapy is illustrated by the following case histories:

A 54-year-old woman with carcinoma of the cecum had lost 31 pounds in weight during a seven-month period, mostly in the two months prior to admission. The hematocrit upon admission was 20. After increasing the blood volume by administration of 3500 cc. of whole blood prior to surgery, the hematocrit rose to 45. For some reason, this patient was able to consume a relatively normal caloric intake. In addition, she received 350 calories daily by tube feedings for all except the first day, 400 calories of Amigen, and 900 calories of Lipomul for two days, 1800 for another two days, and 900 the next to last day. The total averaged 4000 calories daily. She gained approximately 6 pounds, her condition became stabilized, and she tolerated surgery well. (See Figure 1.)

A 69-year-old man with carcinoma of the hepatic flexure of the colon had lost 25 pounds in nine months, most of it in the weeks prior to admission. This patient's oral intake was not satisfactory. Tube feedings were instituted, and he was able to tolerate a daily intake of 700 calories by this means (1000 cc. by nightly drips). Amigen was administered, and intravenous fat in the form of Lipomul. The total intake averaged 3000 to 3500 calories, enabling him to increase his weight from 160½ to a maximum of 170½ pounds—a spectacular weight gain. Although fluid replacement had much to do with the weight gain, the patient's general condition unmistakably improved. (See Figure 2.)

There have been some failures. A 79-year-old woman had a massive basal-cell carcinoma. The onset, according to the history, was thirty years previously. She had refused surgery, until she was literally ostracized by her family because of the fungating nature of the lesion which involved the left anterior thorax, the left axilla and the left breast. By cajoling, we persuaded her to ingest 1500 calories on each of the first six days after admission, with tube feedings in addition. She was unable to tolerate Amigen; in several trials, she reacted unfavorably to it. Despite her increased caloric intake, she continued to lose weight. It was decided ultimately that extensive surgery would be impossible because the patient would increase neither her activities nor her food intake. As we fed her by substitution methods,



Oral	1500	1200				
Tube		700				
Amigen		400		800		400
Lipomul IV.		900		1800	900	900
Total Calories	1500	3200	1900	4500	2800	2500
Blood			1000 cc.		500 cc.	

FIG. 2. Six-day presurgical preparation of a debilitated patient by administration of nutritional supplements and whole blood.

her oral intake dwindled, so that nothing was gained; in fact, because of her delicate condition, she was actually losing ground. Therefore, she was returned to her home for radiation therapy.

COMMENT

We have presented what we believe to be a worthwhile method for improving the operability of aged patients. It involves careful preoperative evaluation, the correction of deficiencies, and an aggressive nutritional regimen prior to surgery.

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DISCUSSION

DR. WARREN H. COLE: Thank you, Dr. Harridge. This paper is now open for discussion. Are there any questions?

QUESTION: What about routine gastric analysis?

DR. HARRIDGE: We do not perform that as a usual procedure.

QUESTION: Will you tell us briefly what was used in the tube feeding?

DR. HARRIDGE: I am unable to state it accurately, but various preparations are available—for example, Sustagen. Many patients report an unpleasant

aftertaste from Sustagen even though it is administered through a tube. Our formula combines milk and egg. Dried milk powder can be added to increase the protein content.

QUESTION: How do you determine when the patient is ready for surgery?

DR. HARRIDGE: Because carcinoma is the most frequent cause of malnourishment in these patients, time for preparation is usually limited. There is no laboratory or other method for determining the exact time for surgery. In cases of protein deficiency, a rise in the level of serum protein is a good laboratory indication. In general, however, clinical judgment must be exercised as to when the patient is ready. We try to arrest weight loss, stabilize the patient's condition and if possible, obtain a weight curve directed upward.

DR. COLE: In other words, you like a gain of 4 or 5 pounds, but make no attempt to have the patient regain 35 pounds. Is that correct?

DR. HARRIDGE: That is correct.

DR. COLE: If the patient regains 4 or 5 pounds, he looks much better and unquestionably is in a much better position from the standpoint of operability. Are there other comments?

QUESTION: Why was treatment not started earlier in the 78-year-old woman who had had carcinoma for thirty years?

DR. HARRIDGE: She had refused treatment previously, but she finally wanted treatment because her family was ostracizing her. Obviously, the salvage rate is not good in a situation like that, but this woman looked as though she would live another year or two, and she was about to be thrown out by her family. The lesion had not been massive for thirty years; it was very small at the start.

QUESTION: Is vitamin treatment instituted in addition to protein supplementation?

DR. HARRIDGE: You are right in asking that. We have no definite regimen of vitamin intake, but multivitamin preparations are utilized in the tube feedings and patients receive vitamins if they are able to take adequate oral feedings.

QUESTION: Will you say a few words about geriatric patients who refuse all oral feedings?

DR. HARRIDGE: In some cases, tube feedings are of great value. Usually, one can manage these patients with mild restraints; that is, their hands are controlled so that they cannot pull the tube out. Tube feedings frequently are the only route for providing nutrition.

QUESTION: Have you had any success with Nilevar?

DR. HARRIDGE: We have not used it a great deal.

DR. COLE: We hear much about it, and know that it has some merit. Papers which have appeared illustrate its effect in improving nitrogen metabolism.

DOES THE PENSION MEAN A TICKET TO THE HUMAN SCRAPHEAP?*

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Retirement is a change of life which has serious health hazards for the worker. The change is both economic and social. It marks passage from a life of gainful employment to a brief period of leisure lasting twelve to sixteen years, if he retires at 65.

Successful adjustment to retirement is required if the worker is to avoid a tortured old age of poor health, pain and sorrow.

Keystones to successful retirement are:

1) Good health
2) Adequate economic planning
3) Social activity.

Preparation should begin at least five to ten years before contemplated retirement.

Understandably, retirement is a critical period. It deprives a person of work on which he has depended for social, economic, educational and health benefits. For most of us, work is a way of life. It identifies and links us with society and provides us with friends. Providing meaning and value to life, it is a prop around which we have centered our activities. Retirement ruptures this pattern and frequently results in the loss of social and business prestige.

The problem of retirement is to secure the values formerly brought by work, through play or leisure-time activity. Good lifetime health habits lay the foundation for a healthy old age. In retirement the worker's health may suffer if he adjusts poorly. People who age gracefully—the healthy curious people with continued interests and activities—have always adjusted easily to their environment and do likewise upon retirement. Overly possessive, dependent persons who are unsure of themselves will sometimes find retirement difficult.

One's reaction to retirement depends not only on previous adjustment and need for self-esteem, but also upon how suddenly retirement occurs and what interests and activities can be substituted for work.

During the critical period of readjustment the retiree will react, depending on his habitual way of meeting problems, with anxiety or depression, with irritability or ideas of persecution, with apathy or sickness. Occasionally the response is a frank and obvious suicide attempt. This may be less apparent but just as effective in the form of a so-called accident or a marked, rapid deterioration of health.

The retired person may turn to alcohol for solace and comfort. In a recent survey of accidents to older people, alcoholism proved to be the main cause.

* Dr. Harris' interesting paper is reprinted from "United Paper" with the gracious permission of Henry Paley, Director of Publications, nited Papermakers and Paperworkers, AFL-CIO, CLC.

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Eating may suffer and this leads to nutritional deficiencies. Emotional stresses of retirement may also hurt circulation, raising blood pressure and increasing heart complaints. Thus, retirement may be "bust" as well as "boon" to the worker.

How can the shock of retirement be softened and the lot of the retired worker improved?

The medical field of geriatrics (or aging) is a relatively new one and is steadily uncovering new findings through study and research. There are, however, some general conclusions we can now draw.

PERIODIC HEALTH CHECK-UPS

Good health habits throughout life provide the foundation for a healthy old age. Since there is no sharp line between health and disease, periodic health check-ups will reveal borderline conditions in time to improve health and happiness.

The most critical phase of aging occurs in the two decades from 40 to 60. During this period chronic disabling diseases such as hardening of the arteries, diabetes, kidney disorders, arthritis and high blood pressure appear. If they are detected early enough, preventive measures can eliminate, halt or control them. In old age these same measures may be too late, since the damage has been done and is permanent.

Chances of good health are improved by adequate diet and sufficient physical exercise to maintain one's weight at the level it was during the twenties. A daily intake of protein (meat, chicken or fish), vegetables, fruits, milk and water is necessary. Fat intake should be restricted by curtailing fried or fatty foods. Excessive smoking or drinking is detrimental, although I must admit some old people I see claim smoking or drinking accounts for their good health. Frankly, I would credit a healthy family background and the absence of serious illness for their longevity.

Mental health should not be overlooked. Situations leading to excessive or unnecessary emotional stress or strains should be eliminated or, at least, handled in such a way as to reduce their harmful effects. A little stress which challenges the individual and stirs up his bovine lethargy is healthful. It does not call for tranquilizers. Only when stress is excessive does it become harmful, since it may overtax the person's reserves. This occurs more often in elderly people whose tolerance for stress, heat and cold, overeating and starvation, dehydration and salt depletion is below that of younger people.

Research on aging, which we and others have conducted, indicates that retired workers may retain good physical and mental health into old age. This is especially true when chronic diseases have not developed to aggravate the situation.

With aging, the bodily processes change very slowly and asymmetrically. Many workers are physiologically and biologically younger than their chronologic age. Others, suffering from illness, are older than their chronologic age. In the same individual some organs may be physiologically older than others. Con-

sequently, one person at 65 may be actually physiologically younger than another person who is younger in years.

Research discloses certain variations in the older worker. Keenness of vision begins to diminish at the age of 24 and declines markedly after 50. Depth perception is at its peak between 40 and 50, and then declines. These disabilities show up particularly in tests which emphasize speed and are only partially helped by increased illumination.

Hearing, especially in the high-frequency range, drops off after 65. General muscular strength begins to decrease after 27. At 50 years of age, approximately 82 per cent of the maximum muscle strength remains. Back muscles lose their strength faster than arm and hand muscles. Manual dexterity reaches its peak between 20 and 30 years of age and then slowly declines. At 50 it falls more steeply. Reaction times follow a similar pattern, but not until the age of 70 is the critical point for deterioration in the speed of reaction reached.

Various tests of higher mental function, such as intelligence, memory, reasoning and learning, show tendencies to decline with age. However, the validity of these tests has been questioned, since they have not been weighed properly. They do show the same characteristics of individual differences so basic to the understanding and measurements of abilities at younger age levels. Within the same individual, as well as among individuals, different abilities begin to decline at different ages and at different rates.

Experience, training and familiarity are often assets of older workers which more than overcome any age defects.

Of interest is the psychologic fact that elderly people who continue to work beyond the usual age of retirement have a higher intellectual capacity than those who do not.

These data indicate that all people vary in their abilities and that age is of no scientific value as a yardstick for retirement.

MODERN RETIREMENT PRACTICES

This brings us to the second step to eliminate "retirement shock," reduce the health hazards of retirement and improve the lot of the retired worker. The first was periodic health check-ups. The second is to set up modern retirement practices based on biologic age and work competence rather than on the unscientific, illogical yardstick of chronologic age.

Current retirement practices are classified as mandatory, selective or flexible. According to the definition of the National Committee on Aging, mandatory retirement programs are those in which every worker retires at a specific age with few or no exceptions. This may happen at a so-called normal retirement age or at a specified later age. The age at which full pension benefits become due is often referred to as "normal" retirement age.

Thus age is the sole basis for retirement in a mandatory program. Usually this thermostat for compulsory retirement is set at 65. This arbitrary age setting may be convenient for bookkeeping or statistical purposes, but it is utterly unrealistic from the health standpoint.

Fifty years ago there was very little difference between the total life span and the working life among men. For most workers there was no sharp break from employment into retirement as we know it now.

In 1900 man's average life expectancy at birth was 48.2 years. Today it is above 65 years. Then, 65 represented advanced old age. A person of this age was in poor health. Today, a worker of 65 in good health is the rule rather than the exception because of our improved health standards and medical supervision. His mental and physical faculties are unimpaired and his experience valuable. Such a person is capable of being gainfully employed for several more years at least. He should have this opportunity.

In selective retirement programs, retirement is compulsory for the worker except when management and the union, under certain established conditions, permit an employee to continue after reaching the fixed retirement age. This differs from the mandatory program in that workers are more frequently retained in accordance with some defined procedure.

Flexible retirement programs may have a normal retirement age for pension and other purposes, but the employee works as long as he wants and can be retired for adequate cause only, such as poor health or incompetence.

As a physician I prefer flexible retirement policies which permit older employees to work, if they desire, as long as they are physically and vocationally competent. Such programs keep people active, the key to a successful life and continued good health.

Concerning the two theories of aging,

1) we wear out
2) we rust out,

my experience indicates that more older people land on the scrapheap of poor health by rusting out than by wearing out.

I hold no brief for any specific retirement age, because each worker constitutes an individual problem. In general, a normally aging person can be expected to be able to continue employment on the basis of physical ability and competence at least to age 68. But not all workers need necessarily continue to work until this age. Some may want to retire even before the age of 65 if their pensions and finances are adequate to carry them for the remainder of their life expectancy. Others have to continue their gainful employment beyond the age of 65 for financial or personal reasons.

What is important is that all persons who retire should retire to some planned, continuous activity of high social and educational value. They should have activity providing the status and prestige that work formerly gave them.

Too often people retire from work and go to seed for lack of stimulation. They are the ones more prone to encounter the shock of retirement. Their only recourse may be to find another part-time job which keeps them busy and happy. Many workers past 65 do this to keep occupied and increase inadequate pension and social security income.

Adequate retirement programs recognize that, with greater longevity, illness strikes more frequently and seriously.

The recent National Health Survey in the U. S. pinpoints the concentration of chronic diseases in the middle and later years. Of people between 15 and 44 years, only 8 per cent are limited by chronic conditions; but the rate jumps to 20 per cent between the ages of 45 and 64 and to 57 per cent for those aged 65 and over.

This means that the retired older worker may face greater medical and hospital costs at a time when his income is limited. If he is able to work longer, his income continues and he can better meet these costs, especially since negotiated fringe benefits usually include voluntary health insurance benefits.

Such benefits should be part of the normal provision for retirement as is provided by the Goodrich, Firestone and Goodyear companies under agreements with the United Rubber Workers. Social Security benefits will also help.

PREPARATION FOR RETIREMENT

The third prescription for happy health retirement is proper preparation for retirement. Many companies are beginning to recognize their responsibilities to their retiring personnel. Such a program leads to better employee relations, a better position in the labor market and improved relations with the community. Some experts regard preparation for retirement as important as the training of a new employee.

Pre-retirement counseling may begin as early as five years before retirement. Frequently it starts with a discussion of when and how the decision to retire will be made.

One of the airlines begins with a thorough physical examination. Depending on the medical findings, the whole problem of the employee's abilities and disabilities is then discussed with the physician and the supervisor. Attention is directed to the possibility of continued employment in the same job or in other jobs for which the worker is qualified. Subsequently, detailed information is included about pensions, death benefits, social security life insurance, income taxes and activities after retirement. The program points up the necessity for acquiring interests in addition to his job which will utilize his free time and tend to keep the employee a useful member of his community. Health problems of retired people, medical costs of increasing illness associated with aging, and proper budgeting complete the practical preparation for retirement.

We cannot emphasize too greatly the importance of preparation for retirement. Many of the problems of old age arise from inadequate appreciation by the retiree of what he faces after retirement. Because he has not properly assessed his resources, mobilized his interests, and laid the proper groundwork, he may lose the battle of retirement, becoming not only a problem to himself but to his family and community. His defeat may lead to the development of physical complaints which actually stem from psychologic causes.

Gradually one sees the decline of energy and responsiveness, a waning of initiative and creative imagination, a narrowing of already limited interest, an increase in egocentricity, a certain warping of personality and a sense of helplessness.

The increasing physical and mental limitations, loneliness resulting from loss of friends and relatives, rejection by children, and loss of economic stability accelerate the aging process, produce premature senility and provoke the sometimes expressed, but frequently considered, idea of leaving this unhappy vale.

Fortunately, all is not black as far as retirement is concerned. Many persons weather the storm easily; others adjust with a little more trouble; and others require much help.

Retirement is no problem for creative people who can develop new interests and new friends at all ages. For those who need help, counseling services and other assistance are available in many communities.

Retirement assistance would be best available at the worker's place of employment through a program which might be jointly set up by management and the union. If not available there, the worker can usually obtain retirement information from the adult education program in his city, senior citizen centers, Council of Community Services, the public libraries, the Social Security Agency and other sources. His union's Community Services counselor is another good source of assistance.

As one author said, "There is no shortcut to longevity. To achieve it is the work of a lifetime."

A little foresight and planning will enable the average worker to avoid the health hazards of retirement and retire happily and successfully to a well-earned life of leisure.

THE LABILITY OF BONE MINERAL*

REGINALD V. BENNETT, M.D.

Hot Springs, Arkansas

The concept that the inorganic component of bone is strongly bound to the organic matrix in a relatively static union has been discounted. Apparently, however, a great deal of confirmatory evidence will be needed to establish the newer concept of bone mineral as a highly labile substance and an important reservoir in the maintenance of electrolyte homeostasis.

In this study, animal and clinical experiments were designed to study the influence of hydrogen ion concentration, vitamins, and hormones upon the electrolyte economy. The pertinent literature on the subject is presented in references 1–118.

EFFECT OF HYDROGEN ION CONCENTRATION UPON THE ABSORPTION OF CALCIUM

Eleven adult mongrel dogs were anesthetized with a barbiturate. Segments of the bowel were isolated and flushed with physiologic sodium chloride solution. Calcium was injected, in the form of 5 per cent calcium gluconate, with the pH adjusted to 8 or 3. Serum and urinary calcium values were determined both prior to this injection and ninety minutes after injection. At ninety minutes, the calcium remaining in the isolated segment of the bowel was determined. Table 1 demonstrates the results of this experiment.

It is evident that calcium, regardless of the pH, is absorbed readily from both small and large intestine. Other observations of interest relate to the calcium made available and the subsequent serum and urinary calcium levels.

Five dogs received 1250 mg. of calcium, and 6 received 2500 mg. Less calcium was salvaged from those which had received the larger quantity. Possibly a greater surface area of the bowel accounts for this fact.

Despite the fact that fairly large quantities of calcium were absorbed, the serum in only 1 instance and the urine in only 2 instances showed a significant increase at the termination of the experiment.

EFFECT OF VITAMINS AND HORMONES UPON THE ABSORPTION OF CALCIUM

Six grown mongrel dogs were used. One dog was prepared for three days with desiccated thyroid, 1 with vitamin A, and 1 with calciferol. On the fourth day the dogs were anesthetized. Two untreated dogs were given 200 units of parathyroid extract intravenously, and 1 untreated dog was given 100 mg. of Solu-Cortef (hydrocortisone, Upjohn). Base-line levels of calcium concentration in serum and urine were determined. The jejunum and ileum were isolated, and a dose of 2.5 Gm. of calcium as calcium gluconate-glucoheptonate (pH 8) was injected into the bowel. The results are shown in Table 2.

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TABLE 1

Effect of Hydrogen Ion Concentration Upon the Absorption of Calcium

Dog	Site of Injection	Calcium Injected (mg.)	pH	Before Injection		After Injection		
				Serum calcium (mg./100 ml.)	Urine calcium (mg.)	Calcium remaining in bowel at 90 min. (mg.)	Serum calcium (mg./100 ml.)	Urine calcium (mg.)
1	duodenum	1250	3	11.6	10.4	100.0	11.4	10.4
2	duodenum	1250	3	10.4	10.4	103.3	10.4	10.4
3	duodenum	1250	8	11.6	12.1	162.9	none	10.4
4	duodenum	1250	8	9.6	2.6	126.5	10.8	20.0
5	jejunum and ileum	2500	3	10.0	3.3	39.5	10.0	12.5
6	jejunum and ileum	2500	3	8.7	2.08	51.4	9.6	5.2
7	jejunum and ileum	2500	8	10.0	3.3	37.4	11.8	3.3
8	jejunum and ileum	2500	8	11.7	1.7	36.3	12.4	3.7
9	colon	2500	3	10.0	3.6	46.8	11.8	4.5
10	colon	2500	3	9.5	9.5	61.2	10.9	7.2
11	colon	1250	8	9.5	4.5	127.7	14.5	5.5

The absorption of calcium in these animals was of the same order as that in animals previously untreated with vitamins or hormones (Table 1). Only the dog receiving Solu-Cortef and the one receiving parathyroid hormone showed significant changes in urinary calcium concentration.

THE FATE OF ABSORBED CALCIUM

Since the considerable influx of calcium is not reflected in the serum or urinary calcium, and since it is not reasonable that it remain in the extracellular compartment, logic indicates that it becomes incorporated into bone.

Two adult mongrel dogs were anesthetized, and the femoral veins exposed. One extremity of each animal was isolated from the circulation by means of a tourniquet. A dose of 1 Gm. of calcium gluconate glucoheptonate was injected rapidly into one femoral vein and blood was drawn from the opposite femoral vein at short intervals. At the conclusion of the experiment, both extremities of each animal were disarticulated and the calcium content per unit of bone from each extremity was determined by the wet-ash method. The results are shown in Table 3. The rapid injection of calcium was not reflected in the serum calcium level. However, there was a significant increase in the calcium content of the bone in which the circulation had not been interrupted, indicating that surplus calcium is rapidly incorporated into bone. Possibly bone eventually could be in a sense saturated with calcium, so that body fluids would reflect any appreciable influx of calcium.

EFFECT OF PARATHYROID HORMONE

One theory as to the action of parathyroid hormone is that it produces a phosphate diuresis and that all changes are secondary to this effect. The Ellsworth-Howard test was devised with this in mind, and is still used in the differential diagnosis of so-called pseudohypoparathyroidism.

TABLE 2

Absorption of Calcium from Jejunum and Ileum after Injection of Various Hormones and Vitamins

	Dog 1	Dog 2	Dog 3	Dog 4	Dog 5	Dog 6
Weight (lbs.)	50	34	24	19	25	22
Serum Ca (mg. 100 ml.)	8.6	10.5	10	11.3	10	10.8
Urine Ca (mg. 100 ml.)	3.2	2.5	11.3	8.6	3.3	4.5
Bowel Ca (Gm.)	2.5	2.5	2.5	2.5	2.5	2.5
Bowel content vol. (ml.)	50	50	50	50	50	50
	Desicc. thyroid, 1 gr. q.d.	Vitamin A 50,000 U	Calciferol 50,000 U	Parathyroid 200 U	Para-thyroid 200 U	Solu-Cortef 100 mg.
Serum Ca	10	10.9	10.5	11.3	9.6	8.8
Urine Ca	5.9	4.1	9.3	6.0	12	15.4
Bowel Ca	475	327.5	405	250	457.5	395
Bowel content vol.	20	30	25	No bowel content obtained. Content of duodenum, 10 ml.	35	47

TABLE 3

Serum Calcium Level Following Injection of 1 Gram of Calcium

	Dog 1	Dog 2
Weight (lbs.)	28	36
Total calcium injected (Gm.)	1	1
Base-line serum calcium level (mg. 100 ml.)	8.7	8.7
Serum calcium at thirty seconds (mg. 100 ml.)	8.7	8.7
Serum calcium at 1 minute (mg. 100 ml.)	8.8	9.1
Serum calcium at 2 minutes (mg. 100 ml.)	8.7	8.8
Bone calcium remaining in circulation, mg. Ca/Gm. of cancellous bone	38.9	37.2
Bone calcium not in circulation, mg. Ca/Gm. of cortical bone	34.8	26.7

A patient with calcinosis universalis and the clinical features of pseudohypoparathyroidism was studied. In addition, 2 normal persons were studied as controls. An Ellsworth-Howard test was performed on each of these 3 subjects. Table 4 gives results of these tests.

No phosphate diuresis was noted within the time allotted. However, an intravenous injection of 200 units of parathyroid hormone frequently will double or triple the amount of calcium and phosphorus excreted over a 24-hour period.

In Table 5 are shown the effects of 200 units of parathyroid hormone intramuscularly upon the 24-hour excretion of calcium and phosphorus. Patient I was a 42-year-old white female with rheumatoid arthritis, receiving 30 mg. of

TABLE 4

Results of Ellsworth-Howard Test in a Patient with Calcinosis and Pseudohypoparathyroidism (Subject I) and in 2 Normal Persons

	Subject I	Subject II (normal)	Subject III (normal)
Phosphate excreted (mg./24 hrs.)			
1 hr.	6.7	11.5	16.7
2 hrs.	6.1	3.6	10.0
3 hrs.		8.1	12.0
200 units of parathyroid hormone intravenously			
4 hrs.	7.3	10.5	12.7
5 hrs.	7.9	12.2	12.2
6 hrs.	6.5	10.5	11.8

Meticorten daily. Patient II was a 55-year-old white male with pulmonary tuberculosis, taking 150 mg. of iproniazid daily. Patient III was a 48-year-old white male with idiopathic osteoporosis or osteomalacia. Patient IV was a 51-year-old white female with hypopituitarism.

It may be seen from Table 5 that the action of parathyroid hormone is not necessarily reflected in the urinary excretion of calcium and/or phosphorus.

The concept that calcium and phosphate ions bear an inverse relationship probably was derived from early studies on rickets; but there is no reason to believe that an anion can bear an inverse relation to a cation. This inverse relationship cannot be verified by the results of injection of either calcium or phosphate into normal persons or those suffering from hyper- or hypoparathyroidism, or by the results of injection of parathyroid hormone.

Since the parathyroid hormone can produce its effect in the absence of the kidneys and of osteoclasts, it is quite possible that the action is upon all tissues and consists of decreasing the number of negatively charged particles.

It seems reasonable to assume that the total electrical charge of the cations will balance that of the anions, and that a deficiency of one ion will result in a deficiency of the other. Such states are seen in calcium-deficiency rickets and in phosphorus-deficiency rickets.

EFFECT OF STRESS UPON URINARY EXCRETION OF CALCIUM AND PHOSPHORUS AND ADRENAL STEROIDS

The effect of adrenal corticoids upon bone is difficult to assess. Although it is recognized that long-term therapy with these agents will cause osteoporosis, this seems to be the result of inadequate matrix formation. The acute effects could not be of this nature.

Three patients in acute stress were studied immediately before and after operation. The first (E. W., Table 6) was a 66-year-old white woman with nonunion of the femur of two years' duration; the second (T. S., Table 7) was a

TABLE 5

Effect of Parathyroid Hormone on 24-Hour Excretion of Calcium and Phosphorus

	Patient I	Patient II	Patient III	Patient IV
Urine volume (ml.)	1260	700	1500	750
Calcium (mg.)	163	177.8	245.5	220
Phosphorus (mg.)	334	385.9	640.6	5.5
200 units of parathyroid hormone				
Urine volume (ml.)	680	950	2465	970
Calcium (mg.)	287.7	104.5	470	342
Phosphorus (mg.)	1390	308.8	942	372

TABLE 6

Patient E. W.

	24-Hour Urinary Excretion						
	Urine vol. (ml.)	Creatinine (Gm.)	Calcium (mg.)	Phosphorus (mg.)	Ammonia (mg.)	17-Ketosteroids (mg.)	11-Oxysteroids (mg.)
Last preop. day	1730	1.0	228	739	475.7	3.6	9.0
First postop. day	265		31.3	169			
Second	1365		161	776			
Third	1135	0.9	227	466.1	215.6	4.1	3.6
Fourth (milk)	905		143	163			
Fifth	900		98.1	150			
Sixth	885	0.6	105	431	221.3	2.5	1.8
Seventh (milk with lysine)	2250		255	857			
Eighth	1570		193	563			
Ninth	2090	0.6	228	676.1	563		
Tenth (milk with hydroxy-l-proline	2390		295.3	353.4		3.3	4.7
Eleventh	2190		179.1	621.0			
Twelfth	850		100.4	218	221		
Thirteenth (milk + 2 Gm. gelatin*)	1460		245.5	367.6		1.5	1.9
Fourteenth	1395		190.1	418.1			

* The main constituents of gelatin are glycine, 26.6% hydroxyproline, 14.6%; lysine, 4.6%; proline, 17.2%; and lesser amounts of other amino acids.

55-year-old white female with a solitary metastasis in the femur; and the third (F. W., Table 8) was a 46-year-old white male with nonunion after vertebral fusion. All were studied for fourteen days after operation, during which time they were confined to bed. After the third day all received one quart of milk a day.

From Tables 6–8, it may be seen that there was no constant relationship be-

TABLE 7

Patient T. S.

	24-Hour Urinary Excretion						
	Urine vol. (ml.)	Creatinine (Gm.)	Calcium (mg.)	Phosphorus (mg.)	Ammonia (mg)	17-Ketosteroids (mg.)	11-Oxysteroids (mg.)
Last preop. day	1675	1.2	228	525	335	3.6	
First postop. day	1000		236	494			
Second	1980		247	679			
Third	1270	1.1	477	586	297.1	3.8	
Fourth (milk)	1500		364	445			
Fifth	1610		336	374			
Sixth	1610	0.7	302	432	249.5	2.4	
Seventh (milk with lysine)	2140		399	320			
Eighth	3100		465	276			
Ninth	1800	0.9	336	315	353	2.6	12.6
Tenth (milk with hydroxy-l-proline)	2510		376.5	276			
Eleventh	2970		432	918.8			
Twelfth (1 qt. milk and 2 Gm. gelatin)	2260		380.1	596.1	350.3		
Thirteenth	3110		452.3	854.7		3.8	9.4
Fourteenth	2595		455.5	802.4			

TABLE 8

Patient F. W.

	24-Hour Urinary Excretion						
	Urine vol. (ml.)	Creatinine (Gm.)	Calcium (mg.)	Phosphorus (mg.)	Ammonia (mg.)	17-Ketosteroids (mg.)	11-Oxysteroids (mg.)
Last preop. day	None						
First postop. day	870	1.0	130.5	450	195.7	4.4	1.9
Second	2375		319	834			
Third	1050		110	314			
Fourth	1450	1.7	178	410	304	5.8	5.9
Fifth (milk)	2530		276	732			
Sixth	2100		153	595.5			
Seventh	2060	1.3	206	522.7	384	7.2	8.6
Eighth (milk with lysine)	2600		248	776.1			
Ninth	1660		188.6	576			
Tenth (1 qt. milk plus 600 mg. lysine)	2105	1.6	229.6	665	433	4.4	11.5
Eleventh	1330		169.2	494.6			
Twelfth (1 qt. milk plus 2 Gm. gelatin)	1950		301.3	743.5			
Thirteenth	1760	1.6	208	604	272.8	11.1	4.5
Fourteenth	2275		446.8	689.5			

TABLE 9

Calcium Adsorption by Bone Chips

	Porosis B.K. W♀ age 51	Porosis E.C. W♂ age 48	Porosis A.J. W♀ age 70	Normal B.S. W♀ age 35	Normal B.A. W♂ age 30	Calcinosis Universalis B.B. W♀ age 23	Normal J.C. W♂ age 29	Normal J.W. W♂ age 25	Porosis V.U. W♀ age 55	Porosis J.H. W♂ age 42	Uremia S.M. C♀ age 36	Porosis A.C. W♀ age 80	Porosis C.C. W♀ age 55	Acromegaly W.S. C♂ age 53
Calcium in A (mg.)	0.057	0.036	0.037	0.037	0.039	0.037	0.042	0.034	0.057	0.090	0.040	0.035	0.035	0.035
Calcium in B (mg.)	0.520	0.485	0.300	0.421	0.500	0.453	0.520	0.445	0.464	0.367	0.408	0.517	0.750	0.545
Calcium in C (mg.)	0.605	0.643	0.277	0.320	0.275	0.255	0.250	0.250	0.262	0.307	0.325	0.205	0.390	0.268
Calcium in bone chips (A + B) − C	−.028	−.122	+.060	+.138	+.265	+.235	+.272	+.229	+.259	+.150	+.123	+.347	+.395	+.311
17-KS excretion (mg./24 hrs.)	3.1	8.5	1.8			15.3			1.9	10.5	0.96	9.4		7.95
11-Oxysteroid excretion (mg./24 hrs.)	4.6	7	3.7			10.7			5.3		6.6	5.0		1.6
Serum PBI (μg./100 ml.)	6.5	9.2	6.5			5.4			9.2	6.7	4.3			6.8

24-Hour Urinary Calcium and Phosphorus Excretion (mg.)
I (water plus 12 Gm. NaCl) II (regular diet plus 200 mg. calcium lactate)
III (regular diet plus 400 mg. calcium lactate)

I	Ca	220	273	143		50		65	46	72		83			354
	P	515	671	360		310		250	250	315		310			1232
II	Ca	345	250	139		150		175	140	60		75			312
	P	372	707	524		350		300	300	402		308			1560
III	Ca	175	201	130		163		150	135	101		53			250
	P	432	600	674		345		375	275	385		238			1302

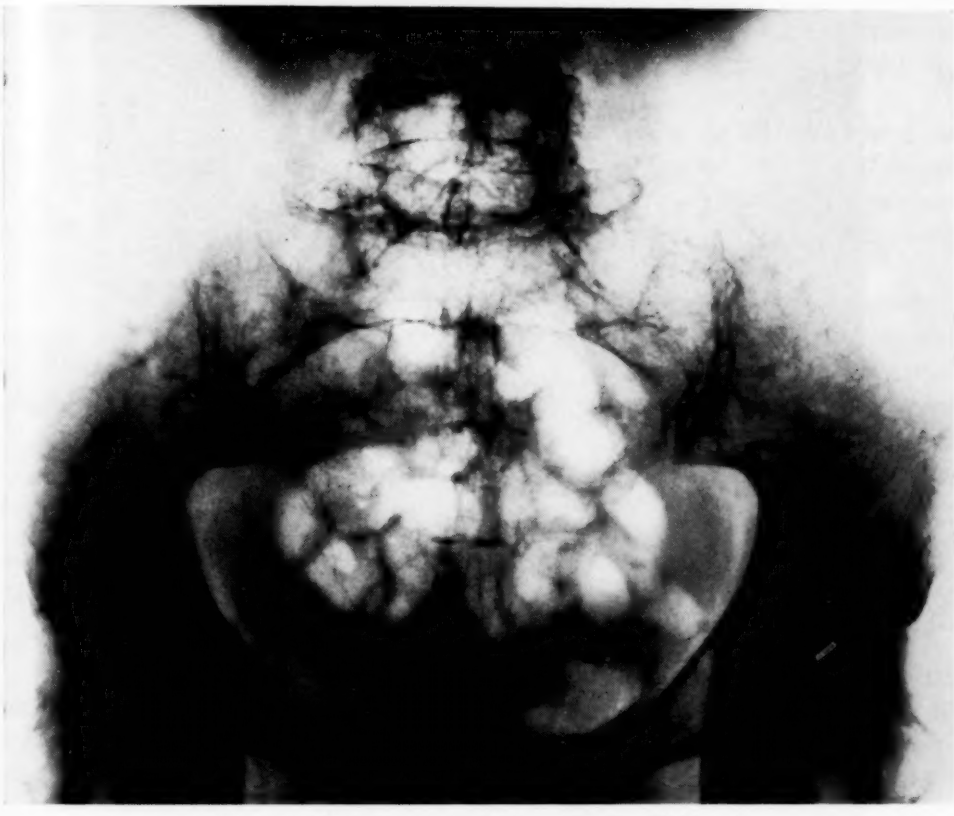

FIG. 1. Osteoporosis in Patient B. K. (Table 9)

tween the amounts of calcium and phosphorus excreted. Neither was there any relationship between the excretion of 17-ketosteroids and 11-oxycorticoids. The urinary calcium fluctuated to some extent with the urinary volume. This is understandable, since calcium is strictly an extracellular ion. This was not true of phosphorus, which bears no relation to urine volume but tends to vary with the excretion of ammonia.

BONE SOLUBILITY

On x-ray examination it is commonly observed that dissolution of bone in various metabolic derangements proceeds most rapidly in the portions of bone that are highly vascularized. It is also inferred on the basis of 24-hour urinary calcium data that the rate of dissolution is by no means constant; for several days urinary calcium excretion may be low, and then suddenly become quite high. The x-ray observations are self-evident. However, the varying rate of dissolution—as deduced from urinary calcium data and from the observation that one bone can be in the process of dissolution while a neighboring bone remains unaffected—is a matter of considerable speculation.

In an attempt to throw some light on this subject the following study was carried out (Table 9). Under sterile conditions, shavings were made of bone from

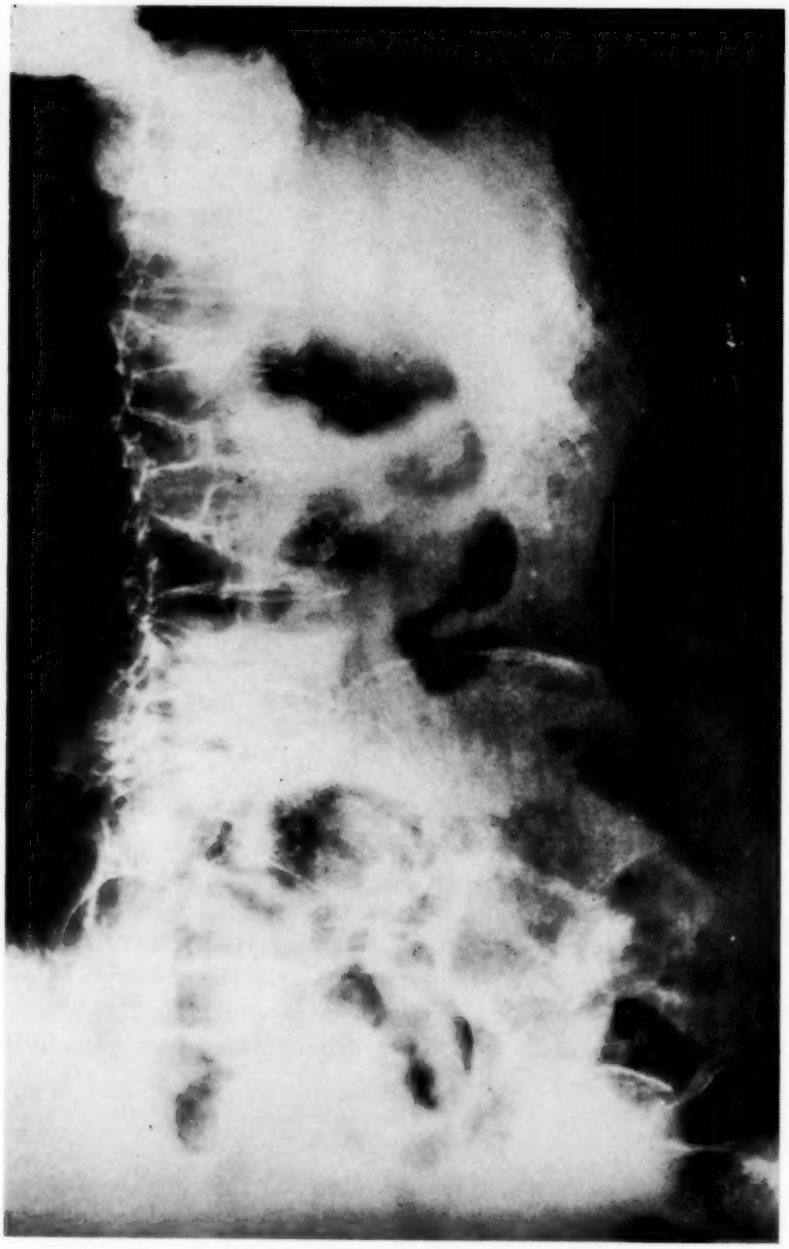

FIG. 2. Osteoporosis in Patient E. C. (Table 9)

4 normal and 10 diseased subjects. The shavings were placed in a flask to which was added 10 ml. of distilled water. The flask was allowed to sit for three days at room temperature. Under sterile conditions, 5 cc. of water was removed from the flask. (Cultures were made, and if positive, the contents of the flask were discarded.) The calcium content of the distilled water was determined. A 5-ml. sample of the patient's serum was then added to the flask, and the flask again was allowed to sit for three days. At this time the total calcium in the 10

ml. was determined. Subtracting this value from the sum of calcium in the distilled water and in the patient's serum gave the amount of calcium which the bone chips adsorbed from the serum.

In only 2 instances did the bone chips give up calcium. In some of these patients the bony changes evident on x-ray examination were quite advanced (B. K., Fig. 1; E. C., Fig. 2). This study indirectly demonstrates the organic and inorganic components in bone formation, and shows that the term "osteoporosis" is descriptive and not diagnostic.

The varying rate of calcium excretion in patients with negative calcium balance bears some relation to the stability of bone mineral. The maturation process of the polyatomic bone crystal is a process of stability rather than instability until it reaches a certain electrical mass, at which time it is closely coated with an ion that not only prevents additional growth but hinders dissolution. Thus at certain levels of maturation the crystal must behave much like an oxide of iron, and at other levels like an oxide of aluminum.

CONCLUSIONS

Bone mineral is a highly labile fraction of the internal environment and reacts rapidly to maintain the balance of electrical particles.

A high dietary calcium is not reflected in urinary calcium; in fact, ingestion of milk along with its essential amino acids tends to lower the urinary calcium excretion. The high incidence of renal stones in paralytics and bedridden patients should be considered in two lights: 1) dissolution of cells with release of a flood of intracellular ionic phosphate, and 2) stasis.

Osteoporosis, as presently used, is a purely descriptive term. The condition may well be the result of an imbalance of electrical particles.

The polyatomic bone crystal during the process of maturation and dissolution must pass through stages of both relative stability and relative instability.

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SYMPTOMATIC TREATMENT OF ASTHMATIC BRONCHITIS

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Several reports have been published attesting to the efficacy of benzonatate (Tessalon)[1] as an antitussive agent when administered in the form of perles (1–3). In tuberculosis, pulmonary fibrosis, emphysema, upper and lower respiratory infections and in artifically produced cough this new drug has apparently been superior to codeine (4–8). Our own work previously had demonstrated that Tessalon in perles, when given to patients with chronic asthmatic bronchitis and pulmonary emphysema in a dosage of 100 mg. three times daily, greatly diminished cough and the amount and consistency of the sputum (9). When compared to another new antitussive drug in these same patients, Tessalon was superior for the treatment of all symptoms related to cough and sputum production (10).

Benzonatate (Tessalon) is a light yellow, viscous, clear liquid and is quite bitter. As it is a long-chain polyglycol derivative—chemically related to procaine—a local anesthetic effect would be expected, and is in fact produced. On absorption, it apparently acts both peripherally and centrally to control cough (11, 12).

It would seem advantageous to add the antitussive agent to a cough mixture rather than give two such medications separately. This paper concerns itself with the results of a double-blind study to assess the value of benzonatate when used in this liquid form.

METHODS AND PATIENTS

Medication

For the last ten years we have used a bronchodilating cough mixture composed as follows:

Ephedrine sulfate	0.5
Ammonium chloride	6.0
Elixir phenobarbital	
Elixir terpin hydrate $\overline{aa}$ q.s.ad	120

This is given in teaspoonful doses every three to four hours as needed for asthma or cough. It seems to be particularly valuable in patients having intrinsic asthma—better named asthmatic bronchitis—as these patients usually cough their way into attacks. A mixture which will ameliorate the racking cough generally aborts an asthmatic attack. We then experimented with the addition of codeine or dihydrocodeinone (Hycodan®)[2] to lessen cough and found the latter superior. It was added in doses of 1 mg., 3 mg. or 5 mg. per teaspoonful of mixture but as no marked differences in cough inhibition resulted, the smallest dose (1 mg.) was continued.

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[1] Tessalon®, CIBA Pharmaceutical Products Inc., Summit, N. J.

[2] Kindly furnished through the courtesy of CIBA Pharmaceutical Products Inc., Summit, N. J.

TABLE 1

PATIENT REPORT

Patient _____ Age _____ R. No. _____ Date _____

Clinical Diagnosis: _____

_____ Duration of Condition _____

	COMPARATIVE RESULTS								
DATE-									
1. Cough:	-	-	-	-	-	-	-	-	-
Frequency - Less									
More									
Same									
Severity - Less									
More									
Same									
Speed of Relief - Faster									
Slower									
Same									
2. Sputum:	-	-	-	-	-	-	-	-	-
Amount - Less									
More									
Same									
Consistency - Lighter									
Heavier									
Same									
Production - Easier									
Harder									
Same									
3. Relief of Tickling in Throat:	-	-	-	-	-	-	-	-	-
Yes									
No									
Comparative Degree									
4. Effect on Breathing:	-	-	-	-	-	-	-	-	-
Easier									
Harder									
Same									
5. Patient's Preference:	-	-	-	-	-	-	-	-	-
A									
B									
C									
6. Side Effects:	-	-	-	-	-	-	-	-	-
No									
Yes (specify)									

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In the present study, the bronchodilating cough mixture was used as a control. To it was added 1 mg. of Hycodan per teaspoonful, and both this mixture and the control were made bitter by the addition of polyoxyethylene sorbitan monolaurate (Tween 20®). These 2 preparations were indistinguishable by taste from the control mixture to which had been added 100 mg. of Tessalon[2] per teaspoonful. All 3 were formulated in the pharmacy and labeled A, B or C. They were prescribed by these letters and the code was known only to the pharmacist until the conclusion of the study.

Patients

Forty-five patients ranging in age from 37 to 72 years (average, 59 years) were selected. Their condition had become stabilized with oral medication and maintenance injection treatment. The A, B or C mixture was started in about the same number of patients. The mixtures were then rotated in turn, so that finally each patient had taken each medication three times. Generally, the four-ounce bottle of each mixture was consumed in one to two weeks per trial. All of these patients had asthmatic bronchitis and pulmonary emphysema. The duration of chronic lung disease was three to thirty-six years, with an average of twenty-one and a half years. Patients with cor pulmonale or hypertension were excluded.

A form was developed (Table 1) to facilitate and standardize the patients' responses to the stock questions asked after they had finished each bottle of medication. A disinterested observer, who did not know the contents of the 3 medications used, queried each patient and recorded the answers.

RESULTS

The results are tabulated in Tables 2 to 5. Regarding frequency of cough (Table 2), only those patients having less cough were listed (since "no effect" or "more" can be grouped together); this applied also to severity of cough and comparative speed of relief. When estimating the effect on sputum, only lessened amount, lighter consistency and easier production were considered important. No significant difference between medications was noted until we considered the

TABLE 2

Control of Cough

Cough	Control Mixture	Mixture with Tessalon	Control Mixture with Hycodan
Frequency lessened	30 (67%)	32 (71%)	30 (67%)
Severity lessened	26 (58%)	28 (62%)	29 (64%)
Acceleration of relief	29 (64%)	26 (58%)	30 (67%)

TABLE 3

Effect on Sputum

Sputum	Control Mixture	Mixture with Tessalon	Control Mixture with Hycodan
Amount less	23 (51%)	21 (47%)	23 (51%)
Consistency thinner	25 (56%)	22 (49%)	25 (56%)
Easier to raise	31 (69%)	33 (73%)	34 (76%)

TABLE 4

Miscellaneous Effects

Symptom	Control Mixture	Mixture with Tessalon	Control Mixture with Hycodan
Throat tickle relieved (11 patients had none)	28 (83%)	29 (85%)	30 (88%)
Respiration easier	35 (78%)	35 (78%)	34 (76%)

TABLE 5

Patients' Preference Regarding Medication

No Preference	Control Mixture	Mixture with Tessalon	Control Mixture with Hycodan
3 (6%)	8 (18%)	12 (27%)	22 (49%)

patients' preference. This preponderance of desire for the control mixture with Hycodan can probably be attributed to the fact that anesthesia of the mouth and tongue was produced by Tessalon. Side-effects were minimal and fleeting and never produced by the same medication on subsequent administration.

DISCUSSION

In searching for an explanation as to why the control mixture resulted in as much benefit as the Tessalon mixture regarding cough and sputum, we must consider the method used. Originally, in assaying the value of Hycodan added to the cough mixture, simple cough preparations were used, such as elixir of terpin hydrate, syrup of white pine, or syrup of wild cherry. We have never been convinced that Hycodan added to our bronchodilator cough mixture was of value, as no patient noted any difference when Hycodan was added or removed. In the cough mixture, the bronchodilator action (which usually includes easier raising of sputum) is due to the ephedrine. The phenobarbital neutralizes some of the side-reactions from ephedrine but probably has little other effect when used in such small dosage. Both ammonium chloride and elixir of terpin hydrate are good expectorants and should cause thinning of inspissated sputum. Thus the only actions on the cough or sputum that could be obtained from Hycodan or Tessalon were already available by means of the other drugs. Although none of these other drugs is an antitussive, they induce easier production of thinner sputum, and this lessens the frequency and severity of cough.

In previous studies using Tessalon perles alone, a good antitussive effect was noted, and there were no complaints due to the buccal anesthesia produced by them.

SUMMARY AND CONCLUSIONS

A double-blind study on the effectiveness of adding benzonatate (Tessalon) or dihydrocodeinone (Hycodan) to a bronchodilator cough mixture showed that there was no significant difference between the control and test medications regarding reduction in frequency and severity of cough or improvement in the amount, consistency and ease of production of sputum, in 45 patients with asthmatic bronchitis. These results are explained by the action of the ingredients of the basic cough mixture in controlling the symptoms of asthmatic bronchitis rather than by lack of efficacy of benzonatate or dihydrocodeinone in controlling cough.

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PROBLEMS IN GERIATRICS*

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Before discussing how medical practice is affected by longevity and early retirement, it might be well to clarify several terms and furnish some basic statistics.

What is geriatric medicine? "Geriatric" comes from the Greek words "geras" meaning "old age" and "atrick" meaning "care of" or "treatment of." In its literal sense, then Geriatric Medicine is the treatment of the aged. This is not to be confused with "senescence," which is the condition of growing old, and comes from the Latin word "senilis" meaning "old."

Today, people in general are living healthier lives and reaching a greater age than formerly. The older group now represents 7.5 per cent of the state's population, whereas in 1890 this group was only 1.7 per cent. We can expect to see the proportion increase to 9 per cent in 1960 and 13 per cent by the year 2000. This notable rise in life expectancy may be attributed to many factors. Striking advances in medical science have enabled the physician to conquer some of the terminal diseases. Relief from economic pressures by old-age pensions and so forth, has helped to prolong life. The use of supplementary vitamins and balanced diets has also played a part.

Let us bear in mind that geriatric medicine is not limited to the senile patient any more than pediatrics is limited to the newborn infant. There is no definite chronologic age among patients at which geriatric medicine begins; it is a matter of anticipation and prophylaxis. Actually, the aging process starts with birth.

VIEWPOINTS IN THE STUDY OF GERIATRIC PROBLEMS

To obtain full comprehension of any problem, it is necessary to study it from 3 distinct viewpoints; otherwise the proper perspective is lost.

1. The problem must be studied as a *unit.* What we are concerned with is human beings; and the misfortunes of human beings have been with us since man began. In early times, the problems of the aged resolved themselves by such factors as disease, war or malnutrition, and resulted in shorter life. People of lower intellect, or those with different moral standards solved their problems differently. For instance, in Africa, when the old people were no longer of use, they were given a spear and one day's supply of food and sent into the jungle. The Eskimos put their old people on ice floes and let them drift away. However, now that old-age security is available, the Eskimo picture has changed. The old people are the patriarchs and it is *their* checks which keep the families provided for during the winter months.

We, being civilized humans, must face our problems differently. One of the

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major changes which has brought the aged to our attention is urbanization. In early days, when people lived on farms and in outlying districts, it was of little concern that grandfather walked about partially dressed, or was incontinent or perhaps a bit "mental," because the nearest neighbor was apt to be a mile down the road. At present, with subdivisions springing up everywhere and one family living practically on top of another, the presence of grandfather is apt to create a problem for society.

2. The problem should be analyzed, and magnification applied to its component parts. Let us keep in mind that we are dealing with male and female, and by their very nature their activities are necessarily different. Women are more used to a sedentary way of life, whereas men must be on the move; they need responsibilities and jobs that occupy the mind. The fact that we are dealing with two sexes further complicates the picture by making it necessary to use separate facilities when the time comes for custodial care.

3. The problem should also be inspected telescopically. Thus we relate the person to his external environment. A close-up view invariably gives a false set of values. For instance, it is important to determine whether the patient is living alone, with his or her spouse, with relatives or friends, or in a public institution. It is also important to know whether his quarters are adequate, and whether or not his presence is creating a hardship for someone, financial or otherwise. Remember the adage: "Two families cannot live under the same roof."

SOME GERIATRIC PROBLEMS

We have to accept the fact that all old people (using age 65 as the base line) have some type of mental or physical impairment ranging from poor teeth to being totally crippled, or from forgetfulness to mental deterioration so complete as to make the person entirely dependent.

1. In many cases, the severity of the disease is greatly amplified by the financial and social situation. Elderly people living with their children often resent the fact that they are dependent upon those children, and consequently they use their ailments as weapons to prevent the family from turning them out. These old people eventually wind up at the doctor's office, having been brought by a son or daughter. History-taking becomes difficult, and physical examinations are slow, tedious, and time-consuming. When the whole underlying problem is ferreted out and presented to the patient, he usually will not accept the fact that he is not seriously ill. The family, feeling the same way, thinks that the doctor does not know his business. The patient is taken from doctor to doctor, resulting in a financial drain on all concerned, but the picture remains the same. Unhappily, however, the trend now is to put old people in institutions rather than to care for them at home. This change can be attributed to the fact that the welfare state is gradually expanding to the point where the state takes over the responsibility for people who have reached government pension age.

2. On the other hand, there are elderly men and women who prefer to be a burden on no one. They live alone on their meager income, stinting on food, living finally in poverty, yet unwilling to move in with their families. They refuse

to see a doctor because they cannot afford it. Eventually, when these people become ill enough and require hospitalization, they are a diagnostic problem as well as a therapeutic one. Associated with their illness (whether it be cardiac, gastric or whatever) is malnutrition; in male patients there is often a urinary condition which may need surgery. Extremely important also is the fact that many of these older people are alcoholics because they have turned to alcoholic stimulants to keep themselves going. They may never get drunk, but they manage to consume enough alcohol to keep a high concentration in their blood at all times. Removal of alcohol from their diet complicates the medical treatment, because in many cases some degree of delirium tremens has developed. Another important factor is that these patients frequently lose their will to live. This is more common in old Italians, who feel that the hospital is the last stop to the grave.

3. Next let us consider a small but troublesome group who are apparently in good mental and physical health, but who have so much time on their hands that they use the doctor's office as a social meeting place. Here they spend hours talking about minor complaints, and taking a long time to dress and undress for examination. This is especially noticeable since the advent of the recent medical assistance program. Although nothing is actually done for this group, the fact that the doctor has listened to their complaints and examined them has a psychologically beneficial effect.

4. A group which includes all types previously mentioned, is composed mainly of patients with malignant or pre-malignant conditions. For example, we see many older people who have an obvious cancerous lesion in the breast. The lesion is small and usually slow-growing. Here the doctor is faced with the choice of whether or not to operate; and, when operation is necessary, whether to perform a radical mastectomy or a simple mastectomy. There are arguments for and against, but regardless of what is done, the doctor wonders if his decision was right. The problem becomes much more difficult when, for example, one is considering a suspicious lesion found on x-ray examination of the stomach. The question is whether the lesion is a benign ulcer or a malignant growth. Should the patient be subjected to the shock of surgery? Should the patient undergo complete removal of the stomach or just excision of the lesion? Should a bypassing operation be performed if an obstruction is present, or, worse yet, should a block dissection of the area be carried out, even though this operation has a high mortality? Naturally, the answers to these questions are not stereotyped, but vary with each case. The decision regarding what to do may be partially solved by the patient—perhaps he is old for his years, or has complicating heart disease, or the cancer has spread from its primary site throughout the body. Nevertheless, the most difficult decision is the one the doctor must make, based on the history and physical findings.

5. Another geriatric problem concerns the amputation of gangrenous extremities. Regardless of whether the patient is diabetic or arteriosclerotic, the situation remains the same. An older person may refuse to have a leg amputated, even though it is making him ill because of toxic absorption. If, on the other hand, he

does agree, he may want to have only a toe or foot removed. This is not enough. If the amputation is to be performed, it must be above the knee, the reason being that the circulation is poor and a low amputation would necessitate repeated surgical procedures ending in amputation above the knee anyway. The medical problem here is obtaining the confidence of the patient and convincing him of what is necessary.

6. Before leaving the subject of medical problems, one more must be considered, not because of its medical seriousness but because of the fact that it makes a dependent person out of a normally independent one. This problem is the broken hip. A fracture of the neck of the femur (or trochanter) is a common fracture in old people, and may result from a simple slip or fall. The fracture must be nailed, but this procedure in itself is simple and creates a minimum of shock. Usually within twenty-four hours after surgery, the patient is sitting up in a chair. The problem arises because upwards of 75 per cent of these old people will never be able to walk or bear weight on the leg again. If the patient is one of the lucky 25 per cent, it will be at least six months before he will be able to walk. The question might be asked "Why is the hip nailed?" This is necessary because, without the nailing, the pain would be so great the patient could not be moved out of bed, and he might die of a complicating cardiac condition.

COMMENT

Many people resent the fact that geriatric medicine is an attempt to prolong life, and feel that there are already too many old people—in short, that longevity has created a burden on the community. Some defeatists imply that the object of geriatric medicine is only to prolong life, and others claim that the object is primarily to relieve suffering. *To the physician, however, the aim of geriatric medicine is primarily to add to the health and usefulness of the aged.* We cannot hope to arrest the process of aging, nor can we expect to prolong the life span of man to any great extent. Aging is part of living; it is the element of time in the process of life.

GASTRO-INTESTINAL DISTURBANCES IN ASSOCIATION WITH METHYLPREDNISOLONE (MEDROL) THERAPY: PRELIMINARY OBSERVATIONS

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Methylprednisolone, synthesized in 1956 (1), has proved to be an effective antirheumatic and anti-inflammatory agent in the treatment of rheumatoid arthritis (2–4) and systemic lupus erythematosus (5, 6). In our initial report on clinical trials with prednisone (Meticorten), we were impressed with the relatively high incidence of epigastric discomfort or dyspepsia. This prompted a review of major gastro-intestinal side-effects in a total of 195 subjects treated during the years 1956 and 1957 (8). Although undesirable gastro-intestinal manifestations were noted in 35 patients (17.9 per cent), steroid therapy had to be discontinued in only 5 (2.5 per cent). Five ulcers were demonstrated—2 radiologically and 3 post mortem.

The present study concerns the gastro-intestinal effects of methylprednisolone in the treatment of rheumatic disease.

METHOD

Methylprednisolone (Medrol)[1] was given orally to 36 patients suffering from a variety of rheumatic diseases and to 4 nonrheumatic subjects who acted as controls (Table 1). There were 21 males and 19 females, ranging in age from 26 to 75 years.

Thirty patients had previously received corticosteroids (including cortisone, hydrocortisone, prednisone, prednisolone or triamcinolone) so that a comparative study of the incidence of gastro-intestinal side-effects was feasible.

Methylprednisolone was given in a divided daily dose, over a period of six weeks to thirteen months (average, 7.1 months). The dosage of methylprednisolone ranged from 2 mg. twice daily to 4 mg. four times daily. The total amount of medication received during the study period ranged from 0.36 Gm. to 3.42 Gm., the average amount being 1.73 Gm. (Table 2).

As in our previous studies, all subjects were questioned as to whether they experienced any gastro-intestinal symptoms such as abdominal pain or discomfort, pyrosis, bloating, regurgitation, nausea, vomiting, diarrhea, and bloody or tarry stools. The occurrence of these symptoms before, during or after a course of therapy with methylprednisolone was recorded. When a positive history of ulcer was obtained, prior roentgenograms, when available, were reviewed. Any past history of tuberculosis, diabetes, emotional disturbance or other pertinent ailments was noted.

Complete radiologic studies of the upper gastro-intestinal tract were carried out by one of us (A.N.) on all 40 patients, usually after four months of therapy, but sometimes sooner if complaints referable to the gastro-intestinal tract required immediate attention. The roentgenologist was not aware at any time of the medication taken by the patients; hence, the element of subconscious bias was kept to a minimum.

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[1] Supplies of this drug were generously furnished by Dr. Hubert C. Peltier of the Upjohn Company, Kalamazoo, Mich.

TABLE 1

Composition of Series

Diagnosis	Number of Cases		Number Previously Treated with Corticosteroids	
	Male	Female	Male	Female
Rheumatic Diseases				
Rheumatoid arthritis	8	14	7	12
Gout	5	—	5	—
Bursitis	1	—	1	—
Rheumatic heart disease or rheumatic fever	1	2	—	2
Degenerative joint disease	2	2	2	1
Lupus erythematosis	1	—	—	—
Controls	3	1	—	—
	21	19	15	15
Totals	40		30	

TABLE 2

Dosage of Methylprednisolone

	Dosage	Duration of Therapy	Total Amount of Drug
Range	2 mg. b.i.d. to 4 mg. q.i.d.	1.5 to 13.0 mos.	0.36 Gm. to 3.42 Gm.
Average	2 mg. t.i.d. or q.i.d.	7.1 mos.	1.73 Gm.

The radiologic diagnosis of ulcer was based on the finding of a crater or a constant deformity, or both. Pylorospasm or coarsening of the gastric or duodenal folds was not considered diagnostic of ulcer.

Urinary uropepsin determinations, gastric analyses for free or total hydrochloric acid, sigmoidoscopy and stool examinations were not performed.

RESULTS

It is of more than passing interest that prior to this investigation 19 patients (47.5 per cent) had symptoms referable to the gastro-intestinal tract *e.g.*, abdominal discomfort, pain or distress, bloating, pyrosis or nausea. Of these 19 patients, 7 had symptoms even before steroid therapy was started. This indicates the difficulty of arriving at conclusions on the basis of *subjective complaints alone.*

Two duodenal ulcers were disclosed after roentgenography. In one instance the patient (Case 1) had no symptoms until she noted tarry stools and progressive weakness and had to be hospitalized for gastro-intestinal bleeding. The other patient (Case 2) had a history suggestive of pre-existing ulcer and had no untoward symptoms during methylprednisolone therapy, but repeat roentgenograms disclosed a duodenal ulcer. Abstracts of their case histories follow.

In this entire study, 11 patients (27.5 per cent) exhibited some form of hiatus hernia upon radiologic examination.

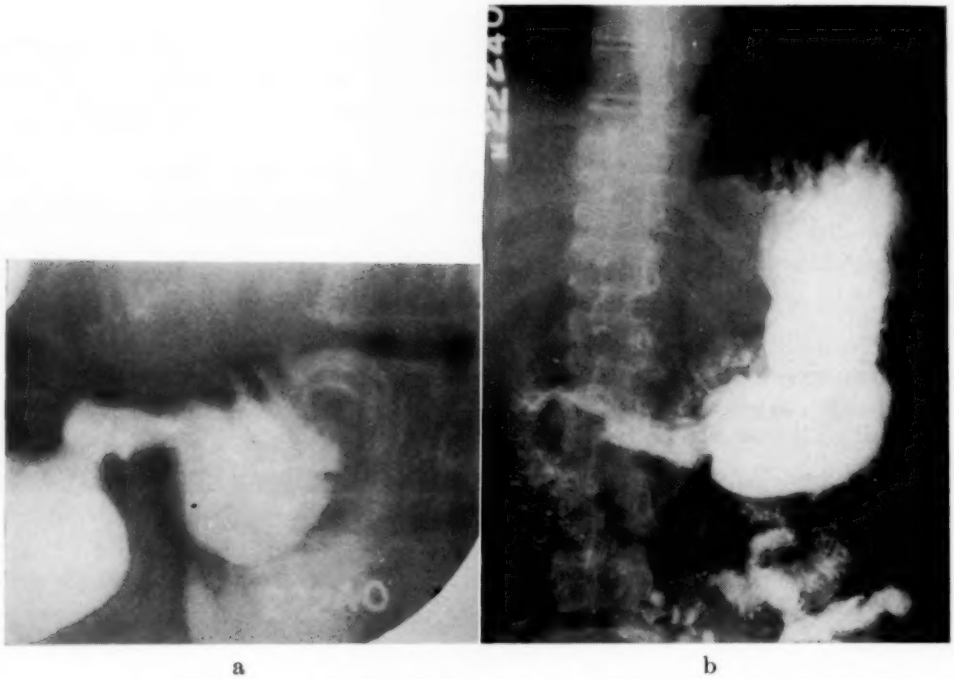

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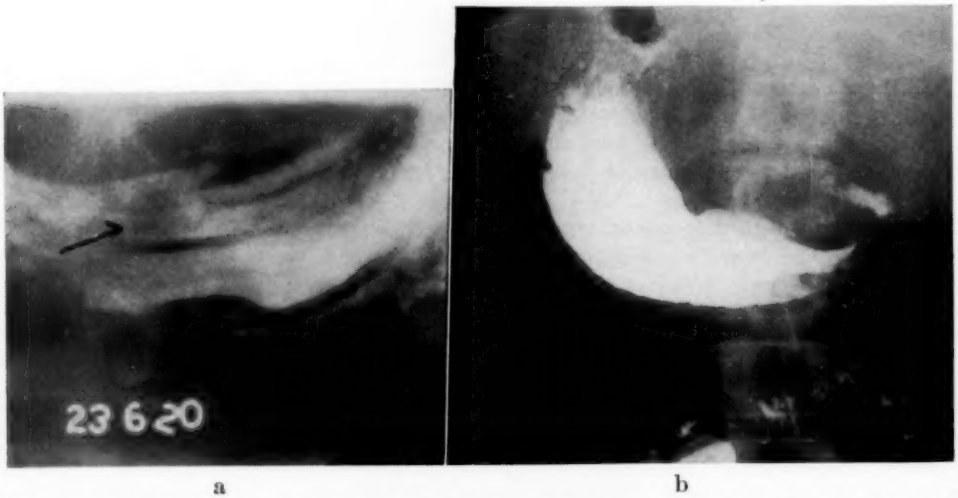
FIG. 1. *Case 1*, after six weeks of methylprednisolone therapy. **a**) *Left*. Active duodenal ulcer. **b**) *Right*. Distinct duodenal ulcer.



a b

FIG. 2. *Case 2*, after nine months of methylprednisolone therapy. **a**) *Left*. Polypoid defect in antrum. **b**) *Right*. Irregularity of duodenal bulb, diagnosis of ulcer.

CASE REPORTS

Case 1

A.S., a 62-year-old woman, had been suffering from diabetes mellitus for five years, but the disease was controlled by diet and sulfonylurea (tolbutamide). Rheumatoid arthritis had developed three years previously and now involved the fingers and wrists of both

a b

FIG. 3. *Case 2*, after twelve months of methylprednisolone therapy. **a**) *Left*. Disappearance of polypoid filling defect. **b**) *Right*. Persistent irregularity of duodenal bulb.

hands—stage II, class II (American Rheumatism Association classification). Methylprednisolone (Medrol) was started in a dosage of 2 mg. four times daily. Both subjective and objective responses were excellent. After six weeks of therapy unaccompanied by any symptoms, she noted tarry stools and weakness. On two occasions, while doing housework, she felt faint and perspired freely. When seen by one of us (J.R.D.) she was in a state of mild shock. The hemoglobin level was 8.5 Gm. per 100 ml., and blood pressure was 86 mm. Hg systolic and 60 mm. diastolic. She was hospitalized and the medication discontinued. X-ray examination showed a distinct duodenal ulcer (Fig. 1).

Case 2

A.C. was a 54-year-old man who had had rheumatoid arthritis for six years. He had been treated with gold, salicylates, prednisone and hydrocortisone for his joint discomfort. He responded best to methylprednisolone (Medrol) in a dosage of 4 mg. twice daily. He had been suspected of having a duodenal ulcer for ten years and was treated with a bland diet and anticholinergics. During the ten months of Medrol therapy, he experienced no new or untoward gastric or intestinal distress. A gastro-intestinal x-ray series after nine months showed a polypoid filling defect of the antrum and a distinct duodenal ulcer (Fig. 2). Despite further intensive therapy with oral methylprednisolone, there was no activation of the ulcer lesion, clinically or radiologically. The original polypoid filling defect had disappeared after three more months of therapy (Fig. 3).

COMMENT

In evaluating the effects of a new drug, it is difficult or impossible to determine accurately whether symptoms related to the gastro-intestinal tract are true side-effects (9–12). One reason is that such symptoms may appear in the absence of any treatment. Another is that these symptoms may occur with nonsteroidal therapy. Almost 50 per cent of our cases had gastro-intestinal disturbances with other steroids (*e.g.*, cortisone, hydrocortisone), before methylprednisolone was started. Proof of an ulcer having been produced by a steroid can be obtained

only by means of serial roentgenograms of the gastro-intestinal tract, before, during and after steroid therapy, showing healing or disappearance of the ulcer after discontinuation of the medication.

The discovery of a peptic ulcer during corticosteroid therapy is *only presumptive evidence* of an etiologic relationship. The entire idea of a direct causal relationship between peptic ulcer and corticosteroid therapy was recently deflated during the Conference on Steroids held by the New York Academy of Sciences (13). However, we know that an ulcer may form while a patient is receiving corticosteroid or corticotropin therapy. In these instances, the possibility always remains that a so-called "silent" ulcer has existed without signs or symptoms (including x-ray findings) and has become activated or complicated during the use of corticosteroids.

In our series, we found 2 ulcers in 36 subjects with rheumatoid arthritis—an incidence of 5.5 per cent. Among the 3 patients who had a so-called "ulcer history," only 1 (Case 2) had activation of his lesions. In another instance (Case 1), bleeding was the outstanding finding, although there was no previous history or objective findings indicative of ulcer.

SUMMARY

Methylprednisolone (Medrol), an effective antirheumatic and anti-inflammatory agent, was studied in 36 rheumatic patients and in 4 controls over a period of thirteen months. Each subject received an average total amount of 1.75 Gm., in divided daily dosage.

Roentgenographic studies were made in all subjects beginning about four months after the start of therapy. Two duodenal ulcers were disclosed by these studies—an incidence of 5.5 per cent. One case was diagnosed after an episode of gastro-intestinal bleeding. In the other case the patient had a previous history suggestive of ulcer, but there were no clinical signs during treatment with methylprednisolone for twelve months. However, the x-ray findings were diagnostic of duodenal ulcer after nine months of therapy, though they had partially cleared up three months later.

Further studies, over a longer period of time, are needed in order to prove whether or not there is a causal relationship between the development of peptic ulcer and the administration of corticosteroids.

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SENILE RECESSION: A CLINICAL ENTITY?

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At this point in medical history, one problem begins to loom up as a consequence of our conquering the infectious and contagious diseases and establishing better health standards. If during the next two or three decades researchers should succeed in mastering schizophrenia, the viruses, heart disease, cancer, and the major chronic degenerative diseases of the later years, senility may emerge as the major challenge to medical science. In a greatly prolonged life span, senility may, in time, become the chief psychopathologic feature of the human life cycle.

One aspect of senility, namely recession, suggests many potentially profitable studies. Most useful for a general framework is Linden and Courtney's concept of the life cycle, especially the very last phases preceding dissolution and death (1). Medical and psychologic theories regarding recession need to be tied to the observation of reality. Since we are still in the early stages of fact gathering, it may be necessary to assemble observations under a few headings, before drawing up working hypotheses.

As a working definition, Linden's (2) will be employed:

> "In recession, the aged person appears to proceed through a series of retrogressive steps through level after level of the infantile development stages all the way back to psychological infantility. In a sense, these are the stages of childhood development up to early adolescence observed in reverse. The last stage of recession is thus the last stage of dementia before death, and corresponds in many ways to foetal and neonatal organization."

THE STAGES OF RECESSION

The following suggested stages of recession constitute a continuous process. Illustrative cases are presented for the purpose of emphasizing the characteristic aspects of each stage. The earlier stages represent psychophysical decline, a turning inward, with a broad ranging from the adult years back to puberty. There is a movement back and forth, involving adult crises, successes and failures. A claim by an older person that he is younger than he actually is, usually means that he has entered into the first stages of recession.

Important phases of the process for society would appear to be puberty, and the four-year to eighteen-month stages. The return to the puberty stage probably helps to explain part of one tragic social problem today, that of the old man who sexually molests young children. These actions often take place as adult ego defenses and adaptations break down, and old sexual strivings are temporarily revived.

The four-year to eighteen-month stage in a child represents dressing ability, and bowel and bladder control (3). A large part of institutional nursing time goes

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into meeting the unusual demands of this stage when recession occurs. Soiled clothing and linens, and the general problem of odor control are the constant concern of harassed Home operators, housekeepers, and hospital administrators.

Stage 1

The onset of senile recession can be observed in the person who begins to reminisce a great deal. There is the fond exploration of pleasant memories, preferably told to an admiring, or at worst, a passively attentive audience. An old crony is quite adequate for this purpose, since by implication he has shared the experiences, and therefore can be assumed to derive a similar pleasure from the re-exploration of familiar grounds.

Mrs. C. D., aged 62, is a frequent visitor to the Home. She is a friendly and gregarious soul, and is extremely helpful to the residents by way of volunteer services. Her favorite pastime, however, is to sit and talk with those of similar background and reminisce for hours on end, discussing the world as it was and the many satisfactions that derive from that period of long ago. Very often she will tell the same story to the same person, completely unaware that she has presented it before. Inflections, intonations, the whole experience will be played as a unit without a real awareness of the audience. Sometimes after sitting for two hours or so, she will get up with a start, feeling very guilty at having spent so much time in this way, and will leave quickly to rejoin the everyday world.

Stage 2

Concomitant with reminiscence, and much more serious as a symptom, is forgetfulness. This marks another break with the world of present reality. Actions are performed mechanically and automatically, while the person is living in a world not quite related to everyday affairs. As a result, many anxieties are generated when a hat is misplaced, a purse or wallet is missing, or some clothing is apparently lost or has apparently been stolen.

Mr. B. A. was a former salesman who was permitted to work despite increasing feebleness, beyond the normal period of retirement. He exhibited slight paranoid trends, most notably about his clothing and personal possessions. Alone among the residents, he kept a special lock on each of his closet doors, carefully locking them every time he left the room. He checked to make sure everything was in place before he closed up; however, even from one time to another, he forgot that he had moved things around in the closet, to make sure that no one could find them. Then when he reopened the closet, he was convinced that someone had moved things since he was there last.

Within three months after being compelled to stop part-time work at 86 for reasons of health, he became a great deal more forgetful. He occasionally accused other residents of meddling with his things. There was extreme suspicion of the maid, and he made double and triple checks on his laundry to make absolutely sure that no clothing had been stolen or lost.

He then lapsed back into his native German, which he had not used actively in his general surroundings for nearly twenty years. Forgetting whom he was talking to, he would enter into long German discussions with members of the staff, and then could not see why they had difficulty in understanding him and his needs. He died at age 87, of pneumonia, after an illness of two months. Time in the institution: five years.

Another case illustrates a tragic symptom of this period, namely, profound

restlessness in the face of deteriorating faculties and a completely frustrating world.

Dr. M. K., a tall, thin, former physician who had retired in his middle 70's, was admitted at the age of 83. He was a good-looking patriarch, friendly, and full of unwanted advice to younger people. Nevertheless, he was frantically in search of the bluebird of happiness, and ran everywhere to find it. During the preceding three years he had moved seven times, from apartment to nursing home, to daughter's home, back to nursing home again, across the U. S., from Texas to Minnesota, to Texas, and finally to Indiana.

His primary irritation was older people. He explained that he, a man of only 65, was too young to have to associate with the aged. After thirteen days, he left the institution for Texas again. He died within six months, following a hip fracture, having lived in three different residences during that time.

Stage 3

As decline continues, withdrawal from the world also progresses. The person often begins to talk aloud to himself a good deal. As the ego defenses crumble, sexual fantasies emerge; regrets and hindsights take over. Small victories are exaggerated into major events. Secret wishes come to the forefront, and loves and hatreds are openly expressed.

Mr. J. S., aged 78, was always interested in obtaining the ear of others for his problems. He would linger in great detail over past events, and especially the times when he had been praised or respected. He always wanted to be considered "among the company of men," implying men of respect and standing in the community. He characterized himself as "humanitarian."

Mr. S. would compare his daughters, leaving the impression that they were little children, not grown women in their 40's and 50's. His greatest wish was to have his wife die first (she was not in the institution), so that he could revenge himself on her alleged infidelities with his youngest son, whom he bitterly rejected, and occasionally suspected was not really his own. He died of a heart attack twenty-one months after admission.

Stage 4

Recession age-period: from puberty back to about 18 months.

Here the tie with current reality is slowly weakened, and a resemblance to some aspects of schizophrenia appears. The person sits quietly alone for hours on end. He stares into space, apparently missing events that are taking place right within visual range. He dozes a great deal, and conversely, wakes frequently during the night. This confusion regarding night and day adds to other uncertainties regarding time and place, and disorientation first appears. Familiar people are confused one with another. Meals are forgotten shortly after leaving the dining room, and accusations of neglect are common at this stage.

Mrs. S. R., aged 83, is somewhat disoriented and seriously deteriorated. From time to time, she will begin to wander away, vaguely in search of something, but with gentle persuasion, she returns. She sits unseeing before movies and television, although her vision is still fair. Her hearing is poor, and this further contributes to her isolated state. Members of her family are not recognized, though one niece, long favored, can convince Mrs. R. of her identity. Three months after admission she began to have an unanticipated bowel movement right after lunch, after the manner of an 18-month-old child. Also, she has begun to lose control of her bladder, and accidents are increasingly frequent. Institutionalization time: two years.

Characteristic of a child aged from 2 to 4 years is a stage when he is continually undressing himself (4). One resident illustrates the return to this stage:

Mr. N. P., aged 81, had had Parkinson's disease for fourteen years before admission. A slight man, he weighed no more than 108 pounds when he came. Both walking and talking presented serious difficulties, and he had a great problem in making himself understood. A year after admission, he began to undress continually. Nothing could dissuade him, and if he were left alone he would strip himself almost completely nude, despite the physical difficulties in the process. This phase lasted six months. He died nineteen months after admission, of cardiac failure.

Stage 5

Recession age-period: from 18 months back to 2 months.

At this stage, the person comes the closest to a second childhood. Often, when he feels threatened or fearful, he cries "Mama." Ego structure is so deteriorated that frequently groaning sounds take the place of speech. Moans and animal cries are uttered, usually in an unending series, broken only by sleep. The person soils himself often, even though toilet facilities or commodes are immediately available. There is disorientation for day and night, familiar people are often unrecognized, and reference points slip away, one by one.

Mrs. S. B., aged 87, was a former founder of the institution, fifty-five years ago. She was active most of her life in community and charity work. Now, she sits in a chair by her bed most of the day. Since it is difficult to eat with utensils, she manages better with her hands. She moans "Ohhhhh, ohhhhh," much of the day, and analgesics and tranquilizers have little effect. There is no immediate memory, and she lives more like a vegetable than an animal form of life. Attendants are needed for almost all activities, and self-help is at a bare minimum. Institutionalization time: three years.

Stage 6

Recession age-period: from 2 months to fetal stages.

As we come into the world, so we go out of it, sleeping and eating intermittently, day and night. Energy levels ebb, and the moans and cries of Stage 5 fade away into a soft "Unhh, unhh," sound that is scarcely audible. Soft or liquid foods are necessary, and milk is the food of preference.

Mr. J. G. was admitted at the age of 87. He could hardly walk, and refused to dress or feed himself, although he permitted the attendants to dress and feed him. A lifelong friend who roomed across the hall, and who loved to reminisce, was usually ignored, as Mr. G. slept between eighteen and twenty hours a day. His favorite food was milk sweetened with sugar, and he insisted on keeping the sugar dispenser in his room so that he could add the sugar to afternoon and evening milk. He was not diabetic. After three and a half months in the institution he passed away due to a severe kidney and bladder infection, complicated by cardiac failure.

At this stage, incontinence is the rule, and the patient goes back into diapers like a baby. He must be fed, too, or starvation and dehydration will carry him off quickly. The eyes close and the lids become sticky and gummy, unless cleaned regularly. The mouth may make sucking motions; it becomes dry. The tongue becomes red and irritated due to oral breathing and avitaminosis. The knees and elbows draw up, the spine curves forward, the head turns inward, and the shell

of the person that is left resembles nothing so much as the caricature of an overgrown fetus.

Mrs. T. K. had retired four years previously from a grocery store which she had managed for decades. She was sent to the institution from a city 115 miles away, making it difficult for her two daughters to visit her. One daughter was relatively normal, if somewhat defensive about her mother's rejecting her. The other, deeply loved by the mother, was passing through an involutional depression that prevented her from meeting her mother's emotional needs. Mrs. K. deteriorated rapidly, rejecting help from the social worker, and refusing to participate in any activity or to relate to anyone other than the Director and the Secretary. Her greatest early institutional satisfaction was to keep the office sponge wet enough to use, although this, too, had to be stopped when it became necessary to mop up after her. Originally, she had an excellent sense of humor, and she half-heartedly tried to expand her knowledge by learning to write English. But these efforts to change over to a new way of life failed. She missed her family, and the brief contacts with her daughters and a deeply-loved nephew were not enough for her family-oriented needs. As recession continued, she passed steadily through Stages 3, 4 and 5. After three and a half years in the institution, she died at the age of 78 in the fetal position, having been bedridden for three months.

DISCUSSION

Several partial and tentative hypotheses can be offered at this time, for working purposes. Concomitants of senile recession are psychologic and physiologic deterioration in most spheres of functioning and a return to prior forms of behavior (5, 6). Further study can rest on two research bases. The first consists of behavioral data on patients who deteriorate steadily, through complete involution. A detailed series of cases is needed, with full histories and descriptive details of the breakdown process. This should include a broad range of psychologic and physical tests and descriptions, whenever feasible. Secondly, the concurrent psychologic characteristics of recession can be studied, with a special analysis of the relationships to childhood forms and modes of thinking. Some work has been done in this area but it is only a beginning (7–9).

Recession can appear concurrently with many other geriatric diseases and conditions. It can occur in schizophrenia, although that psychotic state seems to act as a buffer for some breakdowns of later years. Recession can coincide with severe, moderate or mild arteriosclerosis, and the patient may show the characteristic high variability of mood and orientation. Parkinsonism, cerebrovascular accidents and diffuse organic changes all appear in senile patients. Recession may possibly be a fundamental characteristic of the human life span, and may represent a universal form of psychophysical breakdown. However, certain persons, as for example the late George Bernard Shaw, seem to be almost indestructible psychologically, and continue to live in the present until the time of death.

Are there different kinds of reaction to aging, as Gilbert (10) and others have implied, or is the fountain of youth only a devoted attention to, and involvement with the world of reality? The latter is the thesis of Schuster (11) and most professional gerontologists. This hypothesis may have to be modified, if only because the persons observed did not live biologically to their full term. If they had, perhaps they too might have undergone recession.

Conversely, Linden believes that phenomena of abnormal decline are social rejection artifacts which produce psychophysical deterioration that need not occur during the normal aging process. He implies that the aged person can and should participate in reality and be aware of the needs of everyday existence right up to the end of life. The fact that few people do so simply means that we still have not created the correct social attitudes toward the late aging process.

One of the first signs of recession is a change in memory function. Many psychologists accept the concept that every experience can be totally remembered under the right circumstances, and hypnotic recall tends to verify this thesis. The question remains, however, why memory should be one of the first key functions to surrender. What is there in the nature of the aging process that is so damaging to memory? The physiology of brain function must be understood far better than at present, before answers begin to emerge.

If you ask the early senile patient his age, he tends to get stuck at one recurring figure, *i.e.*, 70, although he is 74; for a while, each birthday is his 70th. Gradually, he begins to announce a younger age. One resident, Mr. J. K., aged 74, when asked his age, said "I think I'm 60, but really I'm 55." Another, Mrs. S. R., aged 83, said "I'm about 30, no more than 35." For the senile patient, all this creates serious confusion about the current date, which may be posted far in the past (*i.e.*, he may querulously say "Is it 1930?") or perhaps some distance in the future ("I think it's about 1973 or so."). The following is an example of an ingenious solution to this confusion:

Mr. M. R., aged 66, had been a victim of encephalitis three years previously. Since that time, he showed moderate recession and confusion as to time, and occasional disorientation for place. To control the erratic and confusing nature of time for him, he would keep a newspaper folded in his belt, inside his jacket. Thus he could glance down, and in a moment have a relatively stable point of reference, namely, the date of the newspaper he was carrying. This paper was often several weeks old, but it was a reassuring point of stability in time.

Some additional research questions can be asked here. For instance: What is the nature of the "hold" mechanism in memory? Why is recent memory more tenuous? Is our perception of time localized in one area of the brain, or is it a total process?

The rate of recession probably varies from person to person; each tends to break down at a different rate. One may degenerate very slowly, showing signs of breakdown over a period of one or two decades. Another may run the entire cycle of degeneration in a year or two. The average would appear to be from two to five years for full senile breakdown, although a large number of patients die of acute or chronic illnesses before the full cycle has been completed.

Recession within the individual apparently can either accelerate or slow down. Not only does the rate vary between people, but it varies within the course of living of a specific individual. Sometimes years may go by, while the person seems to coast at the same level of functioning. Then, based on varying factors, usually external, an acceleration of breakdown and recession will take place. What causes this variability?

Trauma can cause an acceleration, although the process can slow down again after a new stability is reached. In many respects, recession resembles an irregular staircase, with variable height and width of the stairs; but the stairway always leads downward toward dissolution of the personality and death. The nature of the traumatic insults of aging are as varied as the factors in human existence. Primary traumata include physical factors such as infectious diseases, cerebrovascular accidents, diffuse brain changes, variations in blood flow and pressure, and malnutrition. The psychosocial traumata of loss include loss of employment or a key social role, loss of loved ones by death or rejection, loss of old surroundings, and loss of key physical functions such as sight or hearing (12).

In reaction to these traumata of aging, apparently there is not enough energy to adapt completely to the heavy challenge; thus the degree of adaptation that does take place compels the organism to operate at a lower level of efficiency and satisfaction. This, in turn creates new frustrations and irritations, and assists toward further recession. Here is where Selye's concept of the limited total of adaptation energy may be applied. Is the organism really worn out, in a psychic sense, even though physically there may be years of function remaining?

The entire personality does not deteriorate at the same time or the same rate (13, 14). Perception, reasoning and judgment seem to be affected early (15). Thinking moves back to more primitive techniques that had been abandoned years before (16). Insight, however, seems to hold up fairly well. Musical ability, too, may remain intact to some extent. Language ability is maintained in some people, although the basic tendency is downward (17). This ability can form a deceptive facade for much of the deterioration that is present:

Mrs. H. G. spoke well, and gave a much more youthful impression than her 79 years, but her conversation turned in a very narrow circle. When you asked her what day it was, rationalizations would emerge such as: "What's the matter, don't you know?" or "Now that's a silly question to ask!" An elaborate system of rationalizations covered the great holes in her memory and perception system. As a result, she was able to fool the casual observer into thinking that the entire personality was intact. Actually, she knew her name, and very little else. Beyond this, her vocabulary remained intact at possibly the 8- to 10-year old level. She also retained some general information, such as the fact that she lived in the United States. For more than two years, she remained at about this level.

The most important anchor or point of reference in the senile patient is the basic temperament, mood, or outlook. He is himself, only more so. This probably derives from the weakening of ego defenses, and the lessened concern and involvement with the world and its opinions:

Mr. G. G., admitted at age 82, was called "Grandpa" by everyone who knew or dealt with him—his sons, visitors, staff, and the other residents. He resembled in many respects, the ideal picture of what a grandfather should be. Relatively even-tempered and friendly, he was always willing to greet people with a cheerful "Hello," even though he was chair-bound, and had to be helped in all activities. His family and friends reported that during his entire life he had been known for his cheerful, agreeable disposition. Mr. G. retired in 1934, and stayed around the house from then on. He missed his work, and continued to wake at 5 A.M., assuming that he was to go to work at that time, as he had for so many years. Some additional forgetfulness appeared after retirement, but his aging was relatively

normal until the death of his wife in 1950. She had been the focus of his life, and when she died he began to deteriorate steadily. During three years in the institution, his basically cheerful, friendly mood tone remained constant, despite steady senile involution. He died at age 85 from pneumonia.

All the foregoing discussion can lead to several pitfalls if thoughtlessly applied. One of the commonest errors is the assumption that the older person is a child. A return to prior forms of behavior may mean a similarity to certain attitudes and actions of children, but this is far from being a child. The older person has lived a lifetime. A host of experiences have been forgotten, repressed, or integrated into the personality. Condescension, sarcasm and loss of temper on the part of others, are especially hard to bear when one is old, tired, and slightly confused and disoriented. "We know what is right for grandma!" may seem right at the time, but loss of initiative, of self-help and self-care, may be the price of doing too much for the early senile patient. Stated simply, treating the older person like a child helps to push him farther down the staircase of senile recession.

Somewhere during the process of recession a point of no return possibly exists. This is a tentative conjecture, based mainly on experience with senile patients who have not been halted in their decline toward mindlessness and empty memories. A more detailed physiologic and psychologic study of cases would be needed to determine when and if interruption of the final decline can no longer occur. Certainly the techniques of institutional social and group involvement as reported by Donahue and associates (18), Linden (19) and Shore (20), should be applied to senile persons actually experiencing recession. Tests should also be developed to determine if, and at what stage, arrest of the condition has taken place.

What can be done, in a positive way, in the face of psychic collapse and senile deterioration? The work of most therapists emphasizes that a well-integrated total plan works best of all, and that partial techniques can help to a lesser extent. All forms of therapy have a place and a degree of usefulness. Often, a certain technique may work well with one person, and poorly or not at all with another. Seeing each patient as a unique being is one real clue to successful therapy. Then we must find the keys to the patient's personal problem and work at it ceaselessly and ingeniously.

The best therapy is psychiatrically organized, utilizing all resources and techniques. An initial complete organic work-up is essential, since all organic factors such as vascular and coronary insufficiency, tumors and other brain damage, must first be treated with the best medical techniques. Chemotherapeutic tools, particularly the tranquilizers, are a valuable aid at this point in further work, since they serve to dampen or absorb much of the surface anxiety, and permit a facade of normalcy. However, they must never be considered as the final technique in therapy—they are a means, not an end in themselves.

Then psychiatric, psychologic and social work measures can be applied. Group, occupational and recreational therapies, music, intensive social casework, work with the family, out-patient placement, room reassignment, involvement in various forms of activity and responsibility, however limited—all these and other resources can be employed. Hopelessness is the greatest enemy, and apathy is the

destroyer of hope. Ironically, any valid therapeutic technique works to some extent. This merely proves that the senile patient is essentially out of the flow of the life stream. Attempts to bring him back meet with some response in many cases (21):

Mr. A. E., aged 90, had been in the institution for three years. A warm, intelligent person, he was embittered at discovering that he had an endogenous reinfection with tuberculosis at age 85. After two years in a tuberculosis hospital his case had been arrested, and he was transferred to the home for the aged when he was 87 years old. At first Mr. E. participated in programs and, despite crippling arthritis, helped in the cancer bandage program which he had helped to organize while outside the institution. Gradually, he began to express feelings of rejection, ate poorly, lost weight and slept a great deal, often refusing to dress or leave his room. One daughter, very devoted and greatly disturbed by this decline, decided to invest a great deal of time with him. Within a few weeks there was a return to the habits of a year or two before. He left his room, participated in programs, rejoined an outside Bible study class, gained weight and in general was a changed person. This reversal of trend lasted more than a year, with no further decline noted prior to his death from a heart attack at the age of 90.

This does not mean, again, that all therapy should be the same. On the contrary, what may help one person dramatically, may not help another at all. This is helpful in thinking about failures in therapy.

The mood or esprit of an institution sometimes makes all the difference, too, and facilities that provide merely custodial care quickly induce further breakdowns in early senile patients. Treatment-oriented facilities, on the other hand, have a better record of arresting or even reversing recession:

Mr. I. A., at age 78, came to the institution from another city. He had been a tailor all of his life, and had married and raised four children, all of whom lived out of the state. Referred to the institution by an out-of-town agency, he was tired, apathetic and disillusioned, cut off from a lifetime of friends and business acquaintances. In a different community, he relapsed into a self-pitying state of hypochondriasis.

Tuberculosis had been arrested thirty-four years previously. He was anemic, and complained of low back pain. The anemia and a chronic genito-urinary infection were treated medically. Nevertheless, he remained apathetic and disinterested in his surroundings. Intensive personal work with Mr. A. revealed a desire for a sewing machine, so that he could resume his old occupation of tailor. An old machine was used for the down payment on a new one, and Mr. A. agreed to assume the remaining payments, so that the machine could become his. A cutting table, clothes rack, iron, radio, shears, yardstick, and other equipment were all procured. Within a few weeks, Mr. A. was a changed man. He travelled about, first in the neighborhood, then all over the city. Ingenuity and a tradesman's inventiveness emerged. He soon had business cards, and a small business. On weekends, he was the sexton of a small synagogue on the opposite side of town. For five and a half years he remained in equilibrium, keeping active, travelling, and becoming a fixture in the institution and the community. He died at the age of 84, from hepatitis, after an illness of ten days' duration.

In this instance, the right type of institutional attitude made the difference, and reversed the course of senile breakdown. In re-creating a meaningful role in the community, a restoration of social and physical function was produced.

SUMMARY

A theoretic pattern of senile decline is outlined, within the general framework of life development, growth and decline. The phases of decline, corresponding to

the reverse of growth stages in the younger person, are tentatively outlined. Suggestions are made regarding further research and therapy for the senile patient.

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OCCULT MYOCARDIAL INSUFFICIENCY AND PERIPHERAL VASCULAR INSUFFICIENCY: A DIRECT RELATIONSHIP

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In this era of great advances in the development and use of technological equipment, there is still a place for the physician who sees and records. The diagnosis of coronary occlusion prior to necropsy was first made after the invention of the electrocardiogram. A half century later, we are becoming increasingly aware of the limitations of the electrocardiogram (1); it will not show anything until damage to the heart has occurred. An exercise test of the capacity of the heart for the purpose of provoking an electrocardiographic response was introduced eighteen years ago by Master (2, 3). Physical examination of the cardiovascular system is an art yet to be mastered by the average clinician (4, 5). This report concerns clinical observation and experience with the use of a circulation test to aid in verifying the diagnoses of peripheral vascular and occult myocardial insufficiencies.

It has been customary for physicians to separate the diagnoses and also the treatments of impending cardiac catastrophe and peripheral vascular disorders without attempting to establish any relationship between these two disorders, or the interdependence of peripheral vascular disease and heart disease. Recently this relationship has been observed and investigated (6). Richards (7) believes that in many cases intermittent claudication is the first symptom of general cardiovascular disease. Silbert and Zazeela (8) found that the known cause of death in the majority of a series of cases of peripheral vascular disease was either coronary thrombosis (42 per cent) or cerebral thrombosis (12 per cent).

DIAGNOSTIC AND THERAPEUTIC TEST

During the past eleven years I have performed a simple test in the routine cardiac survey of my patients. An injection of 10 cc. of 10 per cent calcium gluconate with 0.5 cc. of 2 per cent procaine hydrochloride is given intravenously to check the circulation time (arm to tongue). By observation of the effects on the peripheral circulation, one can arrive at an accurate estimate of the patient's vascular and cardiac capacity at that time. This test does not preclude x-ray examination, an electrocardiogram and physical examination, but should be done after all conventional types of examinations have demonstrated no findings to explain the patient's symptoms. It should not be performed on any patient if he appears to be undergoing an acute coronary attack, as it will induce shock under these circumstances.

After the injection is given, the patient is asked to tell how far down in the lower extremities he feels a sensation of heat. The correlation between this distance and the circulation time (arm to tongue) is an inverse one. A person with an

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impending cardiac catastrophe will initially have a circulation time of 20 seconds or more (9), and the heat reaction will be felt at some point no lower than mid-thigh. A person without any cardiac or vascular impairment will have a circulation time of less than 12 seconds, and will feel the heat reaction at or below the knees.

Calcium gluconate is used because the resulting heat from irritation of the artery wall, felt subjectively, makes it possible to time the end-point of the test. The procaine hydrochloride is used for its anesthetizing effect on the nerve endings of the artery wall, and to promote dilation of the blood vessels (10, 11). Excellent results have been obtained in the past year by adding 0.1 cc. of Arlidin (5 mg./cc.) to the test solution (12).

RESULTS

The patients studied had occult myocardial insufficiency, *i.e.*, they had (a) symptoms of persistent fatigue despite normal rest, (b) inability to take a deep breath and episodes of yawning or sighing, or both, and (c) nocturia one or more times nightly (usually within three hours after retiring, and with passage of a greater quantity of urine than during the daytime). Their roentgenograms, electrocardiogram, sedimentation rate, and all other physical and laboratory findings were within normal limits, but they had a circulation time (arm to tongue) of 20 seconds or more and passed at least 500–1000 cc. of urine after receiving an intramuscular injection of 0.5 cc. of a mercurial diuretic (9).

The general plan of treatment was as follows: (a) remove the occult edema by conservative use of diuretics, (b) decrease the resistance of the peripheral circulation by the use of intravenous injection of calcium gluconate with procaine and Arlidin until no further improvement can be obtained, (c) restrict smoking, reduce sodium intake, and reduce excess weight to within 5 pounds of the standard weight, and (d) observe the patients periodically to safeguard against recurrence.

A study was made of the effect of this treatment in 50 patients (Table 1) who were followed for periods of from one to eleven years (Table 2). There were 21 males aged 16 to 79 years, and 29 females aged 33 to 72 years (Table 3). Selection of these 50 patients was based on the results of some 2,500 circulation tests.

With the circulation test it was noted that 88 per cent had no feeling of warmth below the hip initially, but after treatment, 80 per cent felt the test-induced warmth at least as far down as the calf (Table 4). Initially only 10 per cent of the patients had edema of the lower extremities, but 60 per cent had such edema at one time or another after treatment (Table 1). The effectiveness of therapy appeared to be independent of age or sex.

In 4 of the patients, before treatment, the circulation time (arm to tongue) after the test injection was 25 seconds or more and there was no feeling of heat below the hips. After treatment, the best circulation time was still 16 seconds or more and the feeling of heat was not experienced below the thigh. Two of these 4 papatients later had coronary occlusions, and 2 had cerebrovascular accidents (Table 1).

The following 2 case reports illustrate the symptomatology, detection, inter-

TABLE 1

Response of 50 Patients with Peripheral Vascular and Occult Myocardial Insufficiencies to Treatment with Diuretics and Vascular Dilators

Patient			Initial Complaints*	Date of Initial Treatment	Cardiac Status at Outset†	Circulation Time, Arm-to-Tongue (secs.)		Cardiac Status after Treatment†	Response to Diuretic‡	Status of Peripheral Vascular Circulation (site of demarcation re warmth)		Edema of Lower Extremities		Complications
No.	Age & Sex	Occupation				First	Best			First	Best	Initial	During Treatment	
1	44 F	Professional	2-3-4-6	June/56	II	22	10	I	×××	Hip	Toes	Yes	Yes	None
2	56 F	School teacher	1-2-3	Apr./58	II	24	15	I	××	Thigh	Toes	No	Yes	None
3	47 M	Laborer	1-7	Aug./57	II	20	12	I	××	Thigh	Toes	No	Yes	None
4	65 F	Housewife	1-2-3-4-6	Nov./53	II	23	12	I	××	Hip	Toes	Yes	Yes	None
5	60 M	Salesman	1-2-3-5-7	Aug./56	III	23	8	I	×××	Hip	Toes	No	Yes	None
6	45 F	Maid	1-2-3	Mar./58	III	19	12	II	×××	Hip	Toes	No	No	None
7	61 M	Jeweler	1-2-3-6	Nov./57	III	18	13	I	××××	Hip	Toes	No	No	None
8	58 F	Maid	1-2-3	Jan./58	III	19	10	I	×××	Thigh	Toes	No	Yes	None
9	67 M	Retired	1-2-3-5	Feb./49	III	23	14	II	××	Hip	Knee	No	Yes	None
10	58 F	Maid	1-2-3-4	Feb./55	II	19	12	I	×××	Knee	Toes	Yes	Yes	None
11	48 M	Salesman	1-2-4	Mar./58	II	22	12	I	××	Hip	Toes	Yes	No	None
12	57 F	Housewife	1-2-3	Dec./54	III	23	12	I	××	Hip	Toes	No	Yes	None
13	59 F	Housewife	1-2-3	Feb./51	III	25	18	Died	××	Hip	Thigh	No	No	Cerebrovasc. accident, Aug./57
14	69 F	Housewife	1-2-3-7	Oct./49	III	35	15	I	×××	Hip	Knee	No	Yes	None
15	33 F	Beautician	1-2-3-4-6	Sept./53	III	23	8	I	×××	Hip	Ankle	Yes	Yes	None
16	51 F	Clerk	1-2-3	May/54	II	25	15	I	××	Hip	Calf	No	Yes	None
17	44 F	Factory worker	1-4	July/52	II	24	12	I	××	Hip	Toes	Yes	Yes	None
18	51 F	Professional	1-2-3-6	June/48	II	21	8	I	××	Hip	Toes	No	No	None
19	73 M	Retired	1-2-3	Oct./57	II	25	15	I	××	Hip	Knee	No	Yes	None
20	49 F	Professional	1-2-3-6	Dec./48	II	26	10	I	××	Hip	Calf	No	Yes	None
21	79 M	Clergyman	2-3-6	Apr./55	II	20	13	I	××	Hip	Knee	No	Yes	None
22	71 M	Architect	1-2-8	Dec./56	II	22	12	I	××	Hip	Toes	No	Yes	None
23	63 F	Housewife	1-2-3-6	Jan./57	II	25	14	I	××	Hip	Calf	No	Yes	None
24	43 F	Housewife	1-2-3	Aug./56	III	25	16	III	××	Hip	Thigh	No	No	Coronary thrombosis, July/58
25	65 F	Housewife	1-2	May/58	III	20	9	I	×××	Hip	Toes	No	Yes	None
26	71 M	Laborer	1-2-3-6	July/52	III	30	14	III	×××	Hip	Knee	No	Yes	None
27	65 F	Maid	1-3	Jan./55	III	28	12	I	××	Hip	Toes	No	No	None
28	46 M	Accountant	1-2	Jan./57	II	28	8	I	××	Hip	Toes	No	No	None

25	65 F	Housewife	1-2	May/58	III	20	9	I	××××	Hip	Toes	No	Yes	None
26	71 M	Laborer	1-2-3-6	July/52	III	30	14	III	×××	Hip	Knee	No	Yes	None
27	65 F	Maid	1-3	Jan./55	III	28	12	I	××	Hip	Toes	No	No	None
28	46 M	Accountant	1-2	Jan./57	II	28	8	I	××	Hip	Toes	No	No	None
29	62 F	Maid	1-2-3-7	Oct./49	III	28	12	I	×××	Hip	Knee	No	Yes	None
30	72 F	Housewife	1-2-3	Apr./58	III	30	15	I	×××	Hip	Toes	No	Yes	None
31	49 F	Housewife	1-2-3	Mar./56	II	20	15	I	××	Hip	Toes	No	Yes	None
32	54 F	Housewife	1-2-3	Feb./53	II	20	12	I	××	Hip	Toes	No	Yes	None
33	68 M	Truck driver	1-2-3	July/57	III	25	15	II	××	Hip	Thigh	No	No	None
34	54 F	House manager	1-6-7	Feb./58	III	24	12	I	××	Thigh	Toes	No	No	None
35	62 M	Superintendent	1-2	Feb./54	III	20	12	I	××	Hip	Ankle	No	No	None
36	53 M	Superintendent	1-2-3-7	Nov./51	II	24	4	I	×××	Hip	Toes	No	No	None
37	40 M	Professional	1-2-3-5-6	Oct./54	III	25	8	I	×××	Hip	Toes	No	Yes	None
38	62 F	Housekeeper	1-2-3-7	Apr./54	III	25	12	I	×××	Hip	Toes	No	No	None
39	71 F	Saleswoman	1-2-3-7	Feb./56	III	26	15	II	×××	Hip	Calf	No	No	None
40	50 M	Clerk	1-2-3-6-7	May/52	II	24	9	I	×××	Hip	Toes	No	Yes	None
41	51 F	Housewife	1-2	Apr./58	II	22	10	I	×××	Hip	Foot	No	No	None
42	67 M	Retired	1-2	Oct./54	II	22	15	II	××	Hip	Toes	No	Yes	None
43	52 F	Professional	1-2-3	Feb./50	III	25	11	I	×××	Hip	Toes	No	Yes	None
44	40 M	Insurance salesman	1-2-4	Jan./53	III	25	19	Died	×	Hip	Thigh	Yes	No	Coronary thrombosis, May/58
45	58 M	Laborer	1-2-3	June/52	III	26	18	II	×	Hip	Thigh	No	No	Cerebrovasc. accident, Sept./58
46	16 M	Student	1-2	Oct./58	II	22	14	I	×××	Hip	Toes	No	No	None
47	75 M	Retired	1-2-3	Oct./57	III	30	12	I	××××	Hip	Toes	No	Yes	None
48	37 F	Maid	1-2-3	Oct./56	III	20	12	I	××	Thigh	Toes	No	No	None
49	51 M	Cook	1-2-3-6-7	Feb./48	II	23	14	I	×××	Hip	Toes	No	Yes	None
50	65 F	Housewife	1-2-3	Mar./52	II	23	10	I	×××	Hip	Toes	No	No	None

* 1 = Persistent fatigue.
2 = Inability to take a deep breath.
3 = Nocturia.
4 = Edema of lower extremities.
5 = Rectal bleeding.
6 = Cold feet.
7 = Intermittent claudication.

† I = Cardiac disorder without limitation of physical activity. Ordinary physical activity caused no discomfort.
II = Cardiac disorder with slight to moderate limitation of physical activity. Ordinary physical activity caused discomfort.
III = Cardiac disorder with moderate to great limitation of physical activity. Less than ordinary physical activity caused discomfort.

‡ Each "×" indicates 500 cc. of urine passed during the hours following injection of a diuretic substance.

TABLE 2
Years Under Observation

No. of years	Males	Females	Total
1	3	6	9
2	5	2	7
3	2	5	7
4	1	3	4
5	3	3	6
6	2	2	4
7	2	2	4
8	1	1	2
9	0	1	1
10	1	2	3
11	1	2	3
Totals	21	29	50

TABLE 3
Age at Onset of Symptoms

Age group (yrs.)	Males	Females	Total
16–39	1	2	3
40–49	5	6	11
50–59	4	11	15
60–69	6	8	14
70–79	5	2	7
Totals	21	29	50

relations and therapy of occult myocardial insufficiency and peripheral vascular insufficiency before the prodromal symptoms have progressed to the easily recognized stage of cardiovascular disease.

CASE REPORTS

Case 1

Although this patient was youngest of the group studied, his is the typical history of fatal coronary occlusion occurring in the second or third decade of life (13). Under some compulsion such as school spirit or military necessity, and lacking obvious physical defect, these young men characteristically continue their physical activity to the point of no return (14). This patient was a basketball player who was tired all the time at home and at school, but was able to play basketball well enough to make the first team.

R. A., a 16-year-old male student, was first seen October 30, 1958, complaining of weakness and tiredness for the previous year, difficulty in breathing for the previous three weeks, and nocturia (twice nightly) for the previous one to two weeks. Initial examination showed

TABLE 4

Results of Circulation Test

Initial					After Treatment						
Circulation Time (arm to tongue)		Peripheral Vascular Feeling of Warmth in Lower Extremities (site of demarcation)			Best Circulation Time (arm to tongue)		Best Peripheral Vascular Feeling of Warmth in Lower Extremities (site of demarcation)				
Time (secs.)	No. of Patients	Knee	Thigh	Hip	Time (secs.)	No. of Patients	Toes	Ankle	Calf	Knee	Thigh
25 or more	20			20	16 or more	4					4*
24	5		2	3	15	9	4		2	2	1
23	7			7	14	5	2		1	1	1
22	6			6	13	2	1		1		
21	1			1	12	16	14	1		1	
20	7		2	5	11	1	1				
19	3	1	1	1	10	5	4		1		
18	1			1	9	2	2				
					8	5	4	1			
					4	1	1				
Totals...	50	1	5	44		50	33	2	5	4	6

* Of these 4 patients, 2 eventually had coronary occlusions and 2 had cerebrovascular accidents.

that the blood pressure was 120/80 mm. Hg, pulse rate 60, and weight 120 pounds. Rales were present in both lung bases. The erythrocyte sedimentation rate was 10 mm. in 60 minutes (Cutler), the hemoglobin level was 14 Gm. per 100 cc., and the white blood cell count was 7,400 per cu. mm. The urine contained no sugar or albumin and the specific gravity was 1.012. A roentgenogram of the chest and an electrocardiogram were normal. The circulation time (arm to tongue) was 22 seconds, and the test-induced warmth was felt to the hip. At this and each subsequent visit, the patient received an intravenous injection of 10 cc. of 10 per cent calcium gluconate with 0.5 cc. of 2 per cent procaine hydrochloride and 0.1 cc. of Arlidin (5 mg./cc.), plus an intramuscular injection of 0.5 cc. of Mercuhydrin. He was instructed to take one 6-mg. tablet of Arlidin daily at bedtime, and to cease all competitive sports for one year.

On November 4, 1958, the patient felt well. All symptoms had disappeared. He passed 1500 cc. of urine within six hours of receiving the Mercuhydrin. Blood pressure was 110/80, pulse rate 60, and weight 122 pounds. When the circulatory test was given, the arm-to-tongue circulation time was 17 seconds, and warmth was felt to the ankles. The Arlidin tablets were stopped, and the patient was told to take one 250-mg. tablet of Diuril every third day.

On November 18, the patient had no symptoms. His weight was 129 pounds. He passed 500 cc. of urine after the injection of Mercuhydrin. Blood pressure was 110/80. Arm-to-tongue circulation time was 15 seconds, and warmth was felt as far down as the toes. He was instructed to take one 250-mg. tablet of Diuril every seventh day.

On December 9, the patient felt well. Blood pressure was 120/80, pulse rate 60, and weight 132 pounds. The circulation time was 11 seconds, and warmth was felt down to the toes. After injection of Mercuhydrin, 200 cc. of urine was passed in six hours. He was told to continue his weekly dose of Diuril.

On January 15, 1959, the patient had no complaints. Blood pressure was 90/60, and weight 135 pounds. After injection of Mercuhydrin, 100 cc. of urine was passed in six hours. The circulation time was 12 seconds, and warmth was felt down to the toes. He was told to stop Diuril and to take instead 12.5 mg. of Hydrodiuril (half of a 25-mg. tablet) every fourteenth day.

On February 17, 1959, the patient had no complaints. The circulation time was 8 seconds, and warmth was felt down to the toes. No extra urine was passed after injection of Mercuhydrin. His weight was 136 pounds. He was instructed to continue 12.5 mg. of Hydrodiuril every fourteenth day.

Case 2

This case illustrates the management and the response of a typical patient with peripheral vascular and occult myocardial insufficiencies but no complications.

C. A., a 56-year-old woman who was first seen on April 8, 1958, had complaints of nocturia (four times nightly) and tiredness for the previous four months, and difficulty in breathing for the previous two weeks. Her blood pressure was 140/120 mm. Hg, pulse rate 88, and weight 159½ pounds. Coarse rales were present in both lung bases, but a chest roentgenogram and an electrocardiogram were normal. The erythrocyte sedimentation rate was 10 mm. in 40 minutes (Cutler), the hemoglobin level was 14 Gm. per 100 cc., and the white blood cell count was 5,200 per cu. mm. The specific gravity of the urine was 1.014; there was no sugar or albumin and the microscopic findings were negative.

At this and each subsequent visit, the patient received an intravenous injection of 10 cc. of 10 per cent calcium gluconate with 0.5 cc. of 2 per cent procaine hydrochloride and 0.1 cc. of Arlidin (5 mg./cc.), plus an intramuscular injection of 0.5 cc. of Mercuhydrin. The arm-to-tongue circulation time was 24 seconds, and the test-indueed feeling of warmth reached the thigh. She was given ammonium chloride (7½ grains three times daily) for one month, and a salt-free diet.

On April 11, 1958, the patient had no complaints. Nocturia was three times nightly, her weight was 161½ pounds, and breathing ability was improved. After injection of Mercuhydrin, 1000 cc. of urine was passed in six hours. Blood pressure was 140/100 and pulse rate 72. The circulation time was 21 seconds, and warmth was felt as far down as the knees.

On April 14, 1958, the patient had no complaints. Nocturia was twice nightly, her weight was 157½ pounds, and the lungs were clear. After injection of Mercuhydrin, 1000 cc. of urine was passed. Blood pressure was 136/96, and pulse rate 72. The circulation time was 15 seconds, and warmth was felt down to the toes. Edema of the ankles had developed.

On May 1, 1958, the patient was symptom-free. There was no nocturia. Blood pressure was 130/90, pulse rate 60, and weight 155 pounds. After injection of Mercuhydrin, 300 cc. of urine was passed. The circulation time was 15 seconds, and warmth was felt down to the toes. Edema of the ankles was less than on the preceding visit. She was scheduled for monthly return examinations until December 1958, and the dosage of ammonium chloride was reduced to twice daily.

On December 8, 1958, the patient was still symptom-free, with no nocturia. Blood pressure was 110/80, pulse rate 60, and weight 153 pounds. After injection of Mercuhydrin, 100 cc. of urine was passed. There was no edema of the ankles. The circulation time was 14 seconds, and warmth was felt down to the toes. Ammonium chloride was stopped, and the patient was instructed to take 250 mg. of Diuril every seventh day.

At the time of the last examination on February 24, 1959, the blood pressure was 110/70, pulse rate 72, and weight 154 pounds. The circulation time was 12 seconds, and warmth was felt down to the toes.

The patient had been taking Diuril 250 mg. once a week, and had had no restriction of diet since December 1958. She has remained symptom-free, and is now being seen every other month.

SUMMARY

Analysis of these results shows we cannot expect our treatment to reverse completely any long-continued malfunction of tissues and organs which disease or misuse may have damaged irreparably. Sometimes very little more than an improved sense of well-being and prevention of further damage can reasonably be expected. The maximum functional improvement which can be obtained under optimum conditions in the individual patient cannot exceed the limits imposed by the patient's own heredity and aging cardiovascular system.

The direct relationship between occult myocardial insufficiency and peripheral vascular insufficiency is shown through the results obtained by a simple clinical circulation test whereby it is possible to define cardiac and vascular potentials.

Data are presented on the results of treatment in 50 patients who were observed over periods varying from one to eleven years. The present therapy for this syndrome is presented in detail for 2 patients.

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THE SKIN DISEASES FOUND IN A HOME FOR THE AGED

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In November 1953 I had the opportunity to examine all of the residents at the Home for the Jewish Aged located at York Road and Somerville Avenue in Philadelphia, Pennsylvania—a constituent of the Federation of Jewish Philanthropies.

TABLE 1

Incidence of Skin Disorders Among 125 Females in a Home for the Aged

Skin Disorder	No. of Cases	Per Cent
Angioma	81	64.9
Fibroma	71	56.8
Seborrheic keratosis	47	34.4
Senile keratosis	35	28
Onychomycosis	28	22.4
Verruca digitata	15	12
Verruca vulgaris	14	11.2
Epidermophytosis	14	11.2
Intertrigo	13	10.4
Sebaceous cyst	11	8.8
Seborrheic dermatitis	11	8.8
Venous ectasias	10	8
Weaver's bottom	9	7.2
Leukoplakia	7	5.6
Neurotic excoriations	6	4.8
Xerosis (moderate severity)	5	4
Eczema (chronic)	5	4
Xanthelasma	5	4
Vitiligo	4	3.2
Lipoma	4	3.2
Fordyce disease	3	2.4
Epithelioma	3	2.4
Eczema (contact)	2	1.6
Lichen simplex chronicus	2	1.6
Purpura	2	1.6
Schamberg's disease	1	.8
Psoriasis	1	.8
Herpes zoster	1	.8
Furuncle	1	.8
Tinea versicolor	1	.8
Cheilitis	1	.8
Sarcoid	1	.8
Granuloma annulare	1	.8

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The home is a modern structure, housing 235 adult men and women and offering the finest in living, dining, recreation and workshop facilities. There were 138 females and 82 males living in the home at the time. Thirteen women and 4 men refused examinations. Thus, 125 females and 78 males were surveyed. The examinations were completed in a period of one year. These residents were examined thoroughly and the diagnosis made on clinical findings alone. A case of sarcoid was confirmed by biopsy. The persons examined were from 65 to 100 years of age and were, as a whole, a group of "healthy" aged. Many were markedly limited in their activities and some were subsequently confined to the infirmary for varying periods. At the time of examination they were permanent residents of the Home, but were free to shop in the neighborhood, visit any part of the city, and remain away for any length of time. The Home was open to visitors at all times. Thus it may be assumed that the residents, while leading a fairly sheltered life, were exposed to most of the usual contacts of everyday life.

In Tables 1 and 2 are listed the skin diseases observed, the sex distribution, and the percentage incidence. The duration of the follow-up period was six years.

TABLE 2

Incidence of Skin Disorders Among 78 Males in a Home for the Aged

Skin Disorder	No. of Cases	Per Cent
Angioma	54	69.2
Fibroma	35	44.9
Venous ectasias	25	32.1
Seborrheic keratosis	24	30.8
Onychomycosis	21	26.9
Seborrheic dermatitis	17	21.8
Weaver's bottom	15	19.2
Senile keratosis	14	17.9
Neurotic excoriation	11	14.1
Epidermophytosis	10	12.8
Fordyce disease	10	12.8
Eczema (chronic)	10	12.8
Sebaceous cyst	9	11.5
Intertrigo	9	11.5
Xerosis (moderate severity)	9	11.5
Schamberg's disease	7	9
Leukoplakia	6	7.7
Verruca digitata	6	7.7
Verruca vulgaris	4	5.1
Epithelioma	4	5.1
Xanthelasma	3	3.8
Lichen simplex chronicus	3	3.8
Lipoma	2	2.6
Furuncle	2	2.6
Eczema (contact)	1	1.3
Moniliasis	1	1.3
Tinea versicolor	1	1.3
Purpura	1	1.3
Tinea cruris	1	1.3

COMMENT

The low incidence of malignant lesions of the skin is misleading, since many epitheliomas had already been removed from these aged persons on admission to the Home and prior to the beginning of this survey. The incidence of herpes zoster was similarly affected. Several post-herpetic scars were noted and 1 patient had intractable pain for two years.

There was a paucity of acute dermatologic conditions until about one year ago, at which time a sharp increase in superficial pyodermias occurred. This was coincident with a general city-wide rise of staphylococcic infections which at times assumed epidemic proportions.

In the entire six years of the survey, no scabies was noted. Herpes simplex was an uncommon finding. Currently there are 2 cases of Kaposi's sarcoma in the Home.

Abstracts of Current Literature

VITAMIN A TOLERANCE TEST AND FAT METABOLISM DISORDERS IN ANGINA PECTORIS.

Beaumont, J.-L., and Lenègre, J. *Am. Heart J.* **58:** 163 (Aug.) 1959.

Vitamin A tolerance tests were performed on 54 anginal patients with coronary atherosclerosis. In 26 of them the curves were within normal limits, in 5 they were below normal, and in 23 they were above normal. Normal curves were found in 7 patients with primary hypercholesterolemia (2 of whom had tendon xanthoma) and in 19 other patients (of whom 8 had a normal blood lipid pattern and 11 had an atypical one). Flat curves occurred in 2 patients with diabetic hyperlipemia and in 3 with an atypical blood lipid pattern. High curves were found in 1 patient with myxedema and in 8 patients with primary (essential) hyperlipemia, but also in 4 with normal blood lipids and in 10 with an atypical blood lipid pattern. The different responses to the vitamin A tolerance test confirmed the presence of different metabolic disorders underlying the various hyperlipemias associated with coronary atherosclerosis. The high curves found in 22 patients (excluding the one with myxedema) are probably related to a disturbance of the early stages of lipid metabolism (absorption, transport, storage). The variable intensity of this disturbance, essentially limited to the postabsorptive period, probably accounts for the divergent results of the simple dosage of fasting blood fats. Perhaps the majority of these cases are representative of different aspects of essential hyperlipemia of variable severity. It is justifiable therefore to detect among anginal patients those with abnormally high vitamin A tolerance curves, thus allowing for a more specific treatment. (Authors' summary.)

DIE LOKALE ANWENDUNG DES ULTRACORTENOL BEI DER KONSERVATIVEN BEHANDLUNG CHRONISCHER LUNGENABSZESSE. VORLÄUFIGER BERICHT. (THE LOCAL USE OF ULTRACORTENOL IN THE CONSERVATIVE MANAGEMENT OF CHRONIC PULMONARY ABSCESS. PRELIMINARY COMMUNICATION).

Bross, W.; Aroński, A.; Moszozyński, L., and Rogalski, E. *Praxis* **48:** 348, 1959; through Ciba Literature Review **4:** 264, 1959.

Until a short while ago the only way to treat chronic pulmonary abscesses was to operate because a thick capsule of connective tissue, impermeable to antibiotics, forms around the abscess in the course of the disease. The intrabronchial instillation of antibiotics in combination with hyaluronidase has now improved the prospects of conservative therapy. The pronounced anti-inflammatory and sustained local effect of Ultracortenol (prednisolone) prompted the authors to use it in combination with antibiotics in the management of chronic pulmonary abscesses. To 7 patients, 10 mg. of Ultracortenol together with antibiotics in a total volume of 5 cc. was administered every second day through a Metras catheter under local anesthesia. The catheter was introduced under x-ray supervision. Heavy accumulations of pus, when present, were drained before administration of the drugs. A complete recovery was achieved with this treatment in 5 cases, and the other 2 patients improved. Ultracortenol is suitable not only as preoperative medication, but also for the conservative treatment of these abscesses.

DIGOXIN: SINGLE VERSUS DIVIDED DAILY MAINTENANCE DOSAGE.

Church, G., and Marriott, H. J. L. *Am. Heart J.* **58:** 171 (Aug.) 1959.

Some patients can be satisfactorily maintained on a higher daily dose of digoxin if the drug is given in divided dosage. To minimize toxicity and achieve optimal maintenance in

the majority of patients, it is best to administer the daily dose in this way. The results of this study refute the recommendation that a single dose is the most satisfactory way to administer digoxin. If adequate control cannot be achieved on this schedule, it is preferable to change to a long-acting preparation.

FOCAL SENILE TRANSLUCENCY OF THE SCLERA.

Cogan, D. G., and Kuwabara, T. *A.M.A. Arch. Ophthalmol.* **62:** 604 (Oct.) 1959.

Focal senile translucency of the sclera is a common finding in old age but it is not known to have clinical significance. The gray color of the areas is due to enhanced visibility of the uveal pigment, but occasionally they contain calcific plaques. An investigation was undertaken of 25 cases and of 30 others examined pathologically. Clinically it was found that the focal areas of translucency of the sclera rarely appear before the seventh decade but commonly are present in persons in the ninth and tenth decades. It has not been proved that they are related to osteoarthritis. The focal areas usually appear as gray spots between the limbus and the tendinous insertions of the lateral and medial recti. They are generally symmetrical in the two eyes. They are sharply demarcated, generally forming a vertical ellipse but they vary greatly in size and extent. No characteristic abnormalities occur in vascularity or in the overlying conjunctiva. When the area is extensive it often contains a calcific plaque. Scleral translucency does not result in perforation, staphyloma, ulceration, or other deformation of the eye. The one pathologic abnormality present in all of the cases examined was a loss of cellularity in the translucent area. The next most characteristic feature was the finding of plaques of calcification in about half of the cases studied. It appeared to be a secondary and late sequela of the loss of cellularity. Crystallography of the calcific plaques was undertaken in 3 cases, since one plaque seen prior to this study had been found to contain calcium sulfate. All 3 were shown to contain calcium phosphate, and a small amount of calcium sulfate was also present in one of them. Fat stains of the areas of focal translucency showed nothing selectively abnormal. Sudanophilia was present in all of the specimens, as is usual in advanced age, but it was not conspicuous in the translucent areas.

GIANT ULCERS OF THE STOMACH.

Cohn, I., Jr.; Sartin, J., and Sudduth, P. *Am. J. Gastroenterol.* **32:** 121 (Aug.) 1959.

A review of the records of 48 patients with ulcers larger than 2.5 cm. in diameter showed that, contrary to accepted belief, the majority of such ulcers are benign. Only 8 carcinomas were present. There are no criteria for differentiating a giant ulcer from the usual gastric ulcer; age, sex, color, x-ray study, gastroscopic study, gastric analysis, location of the ulcer, and the occurrence of complications do not distinguish the two. The incidence of carcinoma in this study agreed closely with the incidence of carcinoma in series of giant gastric ulcers 2.5 cm. to 4 cm. and over in size collected from the literature—carcinoma is present in approximately one-third of the cases in which one cannot be certain whether the ulcer is benign or malignant. Giant ulcers do not respond to medical therapy. Therefore, operation should be performed to alleviate the symptoms and to obtain a histologic diagnosis. It also is indicated because of the susceptibility of large gastric ulcers to perforation, massive bleeding, and pyloric obstruction. The surgeon also may encounter difficulty in making the diagnosis even with the ulcer under direct vision. If there are no obvious metastases, the surgical plan suggested is as follows: once the ulcer has been identified and its relation to other viscera determined, the abdomen is explored for distant metastases. If none is found, the stomach is opened to visualize the ulcer. Although obvious areas of carcinoma sometimes may appear, if the diagnosis still is in doubt a biopsy of the ulcer should be performed remembering that the examination of a single area and finding no carcinoma

does not eliminate the possibility of its presence. Lacking a diagnosis after this, the next procedure is to make an excisional biopsy of any enlarged lymph nodes for frozen section. Examination of the lymph nodes may show carcinoma, but if only an inflammatory reaction is observed, carcinoma still may be present in the ulcer. The surgeon may have to proceed on the basis of inadequate information, and in this situation the finding of this study that giant ulcers are likely to be benign should prove helpful. Without a definitive diagnosis, the resection of multiple organs should not be undertaken. Neither is radical surgery desirable for benign disease. When the entire base of the ulcer cannot be resected without removing other viscera, consideration should be given to leaving its base in situ and adequately resecting the remainder of the stomach or using an exclusion procedure. This approach is desirable because, if carcinoma is present and it has invaded other viscera, the chances of cure are decreased and an extensive procedure is not justified as a palliative measure. However, if the lesion is benign, the patient will have been cured and saved a debilitating operative procedure. Removal of the spleen might be justified, depending upon its accessibility and the patient's condition, but not the removal of portions of the pancreas, liver or colon, nor total gastrectomy.

INHIBITION OF CHOLESTEROL BIOSYNTHESIS IN MAN.

Cooper, E. E. 32nd Scientific Session, Am. Heart Assoc., October 23–25, 1959, *Circulation* **20:** 681 (Oct.) 1959, Part 2.

Because liver adjusts cholesterol production in accordance with amounts returned in the biliary-enteric circulation, inhibition of synthesis is necessary to reduce cholesterol concentration. Reduction of endogenous cholesterol synthesis by a specific inhibitor should therefore produce negative cholesterol balance and mobilize cholesterol from atheromatous plaques. During studies of uricosuric agents, benzmalecene, N-(1-methyl-2,3-di-p-chlorophenyl-maleamic acid (a-isomer), was discovered to inhibit cholesterol synthesis from C^{14}-acetate or C^{14}-*dl*-mevalonic acid by rat liver homogenates. Also, in chronic toxicity studies in dogs, benzmalecene depressed cholesterol levels markedly, and hypercholesterolemia was inhibited in cholesterol-fed chickens. Benzmalecene proved effective in reducing serum cholesterol levels in 14 subjects (male and female, overtly atherosclerotic and normal) studied from two to nine months. The average cholesterol control level for the group was 305.35 mg. per 100 ml.; 500 mg. of benzmalecene was administered in capsules before two or three meals daily (diet unrestricted). Compared to controls, an average drop of 93 mg. per 100 ml. occurred the first week, 103 mg. the third week, 107 mg. the sixth, 96 mg. the twelfth, 63 mg. the twenty-second, 68 mg. the twenty-seventh, and 100 mg. at the thirty-sixth week. No toxic effects were observed in the hematopoietic, cardiovascular or renal systems. Serum bilirubin, urobilinogen and alkaline phosphatase levels were normal. In several patients, there was an increase in bromsulphalein retention, with no jaundice and no bile salts in urine. The retention is interpreted as functional inhibition of the hepatic secretory transport mechanism for B.S.P. (enzymatic activity). Cooperation and tolerance were excellent. In 1 instance there was an evanescent rash. Loose stools were observed twice.

STUDIES ON THE FIBRINOLYTIC SYSTEM AND THE USE OF FIBRINOLYSIN IN ACUTE MYOCARDIAL INFARCTION: PRELIMINARY REPORT.

deLeon, A. C.; Bellet, S.; Tsitouris, G., and Sandberg, H. 32nd Scientific Session, Am. Heart Assoc., October 23–25, 1959, *Circulation* **20:** 684 (Oct.) 1959, Part 2.

Because of the recent interest in the use of fibrinolysin in the treatment of thromboembolic disease, the following studies were performed: 1) plasmin and antiplasmin activity determinations in a group of 28 normal subjects and in 30 cases of acute myocardial infarction (17 without heparin and 13 with heparin), and 2) the use of fibrinolysin in the treat-

ment of acute myocardial infarction (8 cases). Plasmin titers were determined by the whole-clot lysis time, using lysis within twenty minutes or less as an indication of significant fibrinolytic activity. Antiplasmin levels were determined by the clot lysis time produced by 0.2 ml. of 1:10, 1:20, and 1:40 dilutions of 2,000 units of Merck plasmin per milliliter on a preformed clot in the presence of the patient's undiluted plasma. No plasmin activity was noted in either the normal or the acute myocardial infarction groups. The antiplasmin level of the normal group was 211 ± 47 seconds (1:10); 468 ± 146 seconds (1:20); 755 ± 191 + 1 > 1,200 seconds (1:40). In the group of myocardial infarction without heparin the results were 440 ± 231 (1:10); 857.0 + 7 > 1,200 seconds (1:20); 1,095.1 + 11 > 1,2000 seconds (1:40). In the group of myocardial infarction with heparin the values were 364 ± 105 seconds (1:10); 823.7 + 3 > 1,200 seconds (1:20); 1,086.8 + 9 > 1,200 seconds (1:40). It will be noted that the group of acute myocardial infarction taken as a whole had antiplasmin levels significantly higher than those of the normal controls. Human plasmin in doses ranging from 50,000 to 200,000 units was infused intravenously in 8 cases of acute myocardial infarction. In 3 of the 8, pyrexia of over 101°F. developed, and 2 showed a rise in temperature of 1°F. with infusion of the drug. Other side-effects were chills, mild transient hypotension, nausea, vomiting, and flushing. Six of the 8 patients experienced striking relief of angina and 3 showed improvement of the electrocardiogram after infusion of plasmin. These results suggest that fibrinolysin may be an important addition to therapy in selected patients with acute myocardial infarction.

CLINICAL AND ELECTROENCEPHALOGRAPHIC CONSIDERATIONS IN THE DIAGNOSIS OF CAROTID ARTERY OCCLUSION. A REVIEW OF 35 VERIFIED CASES.

Haas, W. K., and Goldensohn, E. S. *Neurology* **9:** 575 (Sept.) 1959.

The clinical diagnostic features of unilateral carotid artery occlusion demonstrated by this study are as follows: preponderance in men, onset predominantly in the fourth to sixth decades, frequent episodic or stuttering progression of symptoms (the syndrome of cerebral intermittent claudication described by Hunt in 1914), a marked tendency for the contralateral upper extremity to be the site of the initial motor or sensory symptoms and of the most profound motor deficit, infrequent involvement of the optic radiations, infrequent complaint of headache, infrequent appearance of seizures either initially or as a sequel to infarction, infrequent presence of high blood pressure, persistence of palpable carotid pulses in nearly all patients, and usually normal cerebrospinal fluid and sedimentation rate values. Arteriography was performed successfully in 27 unilateral and 4 bilateral cases with no change in the clinical status in the latter. Following unilateral studies, a marked increase in focal deficit occurred in 4 instances and persisted in 2 of them. The procedure was unsuccessful in 1 patient with bilateral disease in whom generalized seizures developed. Ventriculography in 1 patient was followed by aphasia, right-sided weakness and generalized seizures, and in another by stupor and increased respiratory difficulty. In 2 of 4 patients, a marked increase in focal impairment occurred following pneumoencephalography. These ill effects contraindicate air studies in cases in which the differential diagnosis includes carotid occlusive disease. The results of electroencephalographic studies are summarized as follows: The abnormalities were primarily of the slow-wave variety, as often observed in cases of brain tumor. Some patients showed focal depression of voltage only. The degree of electroencephalographic abnormality generally paralleled the severity of the neurologic deficit. The frequency of occurrence of electroencephalographic abnormalities in carotid occlusive disease was 83 per cent. Persistent, severe abnormalities often lasted for months to more than a year, especially when the neurologic deficit was marked.

TREATMENT OF ARTERIOSCLEROTIC MACULAR DEGENERATION WITH LIPOTRIAD. A FIVE-YEAR REPORT.

Hilgartner, H. L. *Eye, Ear, Nose & Throat Monthly* **38:** 842 (Oct.) 1959.

Lipotriad in a dosage of 1 to 3 capsules after each meal was administered to 96 patients with macular degeneration. Among 62 with imperfect vision, with no definite retinal changes, and in whom refraction did not improve vision, 70 per cent improved and 30 per cent did not. Many of the patients had blurred 20/20 vision, with vitreous floaters and arteriosclerosis. Patients without floaters in the vitreous responded rapidly, with vision returning to 20/20 or 20/16 in six to eight weeks. Patients with blurred vision of 20/20 and with vitreous floaters improved more slowly. Some patients discontinued medication. A few had gastric distress or diarrhea which necessitated reducing the dosage to 1 capsule after meals, but this amount did not deprive them of benefit. Eighteen other patients had deposits of pigment in the macular region and floaters, but no exudates or hemorrhages; 67 per cent of this group improved, and 33 per cent did not. Lipotriad tended to improve and maintain visual acuity. It did not arrest the gradual development of pigmentary changes in the macula, nor prevent the development of hemorrhages with eventual retinal destruction. It did not reduce blood pressure nor retard progressive changes due to age. Twenty patients had severe central destruction and some of them had exudates and hemorrhages due to thrombi or rupture of the vessels from hypertension; 75 per cent of this group showed improvement, and 25 per cent did not. Conclusions drawn as to the effects of Lipotriad include the following: It does *not* retard or prevent the progressive development of cataracts, prevent the progressive formation of pigment in the macular region or the ultimate destruction of the retina from hemorrhage in patients with hypertension, reduce blood pressure, nor regenerate destroyed optic nerve fibers. It *does* effect absorption of grayish exudates and improve peripheral vision, reduce macular edema, and improve central vision. Lipotriad is more effective in younger patients, and in those with no pathologic changes in the retina other than arteriosclerosis.

ANTIHYPERTENSIVE EFFECT OF SPIRONOLACTONE (SC-9420) STEROIDAL ANTAGONIST.

Hollander, W., and Chobanian, A. V. 32nd Scientific Session, Am. Heart Assoc., October 23–25, 1959, *Circulation* **20:** 713 (Oct.) 1959, Part 2.

Previously reported studies on a spirolactone SC-8109, an aldosterone antagonist, indicated that such compounds might be useful as antihypertensive agents. Therefore, spironolactone (SC-9420), a more potent steroidal antagonist, was studied in 32 hypertensive subjects in daily oral dosages of 150 to 400 mg. Spironolactone alone reduced blood pressure in 6 of 12 hypertensive subjects by 15/10 to 65/35 mm. Hg, but had no hypotensive effect in 10 normotensive subjects. When added to other antihypertensive treatment, it further reduced blood pressure in 15 of 20 subjects by 15/10 to 55/30 mm. Hg. Spironolactone was well tolerated and caused no noticeable serum electrolyte or BUN disturbances. It restored the serum potassium level to normal in all cases in which it had been reduced by chlorothiazide. Metabolic studies in 8 subjects indicated that: 1) Spironolactone blocks the renal excretory effects of desoxycorticosterone on sodium and potassium. 2) The antihypertensive effect of spironolactone is associated with a negative sodium balance of 147 to 258 mEq. and a slightly positive potassium balance of 45 to 98 mEq. 3) A reduction in plasma volume occurs in half the treated cases. However, during spironolactone (as during chlorothiazide) treatment, experimental over-expansion of plasma volume by plasma infusion, or correction of negative sodium balance by saline infusion, does not abolish its antihypertensive effect. Results: 1) Spironolactone is an effective antihypertensive agent which does not produce hypokaliemia, but can correct the hypokaliemia produced by

chlorothiazide. 2) Its antihypertensive effect, like that of chlorothiazide, is not due solely to depletion of body sodium or plasma volume.

LEVOMEPROMAZINE (NOZINAN)—A NEW NEUROLEPTIC AGENT FOR TREATMENT OF SENILE PATIENTS.

Huot, J. M., and Kristof, A. C. *Canad. M. A. J.* **81:** 546 (Oct. 1) 1959.

Levomepromazine was administered to 98 patients with the following disorders: agitation, 30; depression, 22; mental retardation, 13; parkinsonism, 10; mental confusion, 7; schizophrenia, 7; paranoia, 4; anxiety state, 2; miscellaneous, 3. Approximately 80 per cent were past the age of 70 and more than half were over 80 years old. Since the tolerance of elderly patients for this drug is poorer than in patients below age 50, it had to be used in dosages of less than 75 mg. daily. Most of the patients could be maintained on 50 mg. or less, the average being 25 mg. Twenty-two patients required only 12.5 mg. per day. Therapy was continued for two to three months. The effect of levomepromazine, judged by the change in the principal symptom or symptom complex, was considered excellent in 10 patients, good in 51, fair in 14, and absent in 14. The drug had to be discontinued because of intolerance in 9 patients. Good improvement was obtained in the majority of agitated and depressed patients. An appreciable change in behavior occurred in the mentally retarded patients who improved. They became less difficult to manage and better able to carry on their daily activities. With the exception of 2, confused patients grew more sociable, and were less restless, better oriented in space and time, and better adapted to reality. Five of 7 chronic schizophrenic patients became less negativistic, more responsive to normal contact, and showed better coherence and greater activity. Three of 4 paranoic patients showed more flexible behavior. Less favorable results were obtained in parkinsonism, but the reduction in nervous tension and tremor were thought to make trial worth while. Five of the 14 patients without a response had previously improved when given promazine or chlorpromazine. The intolerance that developed in 9 patients consisted of severe drowsiness with general weakness for several days. Five patients had diarrhea. Moderate drowsiness also occurred in several other patients. It is concluded that levomepromazine is useful in senile patients with various nervous disorders.

ROLE OF BLOOD SUGAR LEVEL AND RENAL THRESHOLD (RENAL GLUCOSE CLEARANCE) IN THE ADAPTATION TO STRESS OF AGING.

Lamar, C. P. *Proc. IV Congr. Internat. Assoc. Gerontology* (Merano, Italy, July 1957), Vol. 2, Clin. Div., p. 376; through Excerpta Med. (Gerontol. & Geriatrics) **2:** 245, 1959.

Hyperglycemia is probably a protective phenomenon and, when present without glycosuria, may be a part of the homeostatic adaptation to the stress of aging in certain persons. No evidence exists that hyperglycemia results in harm to the human subject. On the other hand, the time-honored belief that sugar restriction in the diet and insulin administration are needed to restore the blood sugar level to "normal" frequently results in mental and physical deterioration of the subject. "Senile dementia" or "cerebral arteriosclerosis," weakness, mental "fuzziness," confusion and irritability of elderly so-called "diabetics without glycosuria," kept under classic diabetic management aiming at "chemical control," are accepted fatalistically and uncritically as unavoidable and "due to degenerative complications of diabetes mellitus." Many of these patients, forced into retirement and into senility in their sixth decade of life or later, have been rehabilitated and restored to mental and physical normality and to productive, healthy enjoyment of living, by no other treatment than by avoiding interference with their own adaptive mechanisms and letting the blood sugar level be what it may, as long as no ketonuria or excessive glycosuria appears. In the cases of overt diabetes with clinical symptoms and

need for insulin supplementation, doses are adjusted to keep blood sugar levels always slightly above, never far below, the renal threshold. Mild glycosuria acts as a safety indicator and helps prevent hypoglycemia. A low-grade (or "relative") sustained low blood sugar level is frequently the cause of many so-called "senile manifestations in the elderly." When the diet is arranged to contain moderate amounts of sweets and starchy foods at frequent intervals, along with moderate amounts of well digested protein food, avoiding large meals which are too heavy a burden for most elderly people, many senile psychotic disorders clear up that would otherwise not improve under shock or drug therapy. The erroneous interpretation of the role of a high blood sugar level and the rigid concept of "normal glycemia" with insistence upon "sugar-free urine," should be discarded in the light of these observations.

SERUM LIPID AND CHOLESTEROL LEVELS IN CEREBROVASCULAR DISEASE.
Meyer, J. S.; Waltz, A. G.; Hess, J. E., and Zak, B. *A.M.A. Arch. Neurol.* **1:** 303 (Sept.) 1959.

No significant difference was found between the mean serum cholesterol or lipid determinations in a group of 110 patients with cerebrovascular disease and those in a group of hospitalized patients of comparable age with nonvascular neurologic disease. In this series, 12.7 per cent of patients with cerebrovascular disease suffered from diabetes mellitus, but the diabetic patients (who were under therapeutic control) did not have serum lipid or cholesterol values that were significantly different from those in the rest of the group with cerebrovascular disease uncomplicated by diabetes. A group of patients with cerebral atherosclerosis involving the vertebral-basilar, internal carotid, or smaller cerebral arteries did not have mean lipid or cholesterol values that were significantly different from those of a group of healthy men with a mean age of 30 years, but there was a significantly greater percentage of patients with cerebrovascular disease who had elevated serum cholesterol or lipid values. This finding appeared to reflect the tendency of these values to increase with age. A group of patients with developmental and/or diffuse hypertensive cerebrovascular disease (*i.e.*, hypertensive encephalopathy, ruptured aneurysm, or malformation) were found to have significant elevations of serum cholesterol and lipid levels. Since 85 per cent of this group of patients has associated hypertension, it is believed that hypertension may be the significant factor in relation to hypercholesteremia and hyperlipemia. The incidence of all types of cerebrovascular disease, including carotid and vertebral-basilar artery insufficiency, was no different in white and Negro groups, nor was any racial difference noted in serum cholesterol or lipid levels. Atherosclerosis produces cerebral symptoms by involving three major groups of cerebral vessels with approximately equal frequency. Approximately one-third showed evidence of disease in the vertebral-basilar artery system, one-third had symptoms due to disease in the carotid arteries, and one-third to disease in the small cerebral vessels (anterior, middle, and posterior cerebral arteries and their branches). In all types of cerebrovascular disease, the incidence of hypertension is significantly greater than in a group of comparable age with neurologic diseases other than vascular in nature, in spite of the fact that atherosclerotic disease of cerebral vessels commonly manifests symptoms in the absence of hypertension or when a previously elevated blood pressure has fallen to normal levels. Since hypercholesteremia and hyperlipemia probably enhance any tendency toward atherosclerosis of cerebral vessels, the therapeutic use of a low-fat diet in cerebrovascular disease is recommended. (From authors' summary.)

DEVELOPMENT OF CEREBRAL ATHEROSCLEROSIS IN VARIOUS AGE GROUPS.
Moossy, J. *Neurology* **9:** 569 (Sept.) 1959.

Examination of the intracranial portions of the internal carotid and basilar-vertebral arterial systems of 122 patients showed that the vessels of patients below age 20 were not

affected by cerebral arteriosclerosis. From the third decade onward all patients showed some degree of cerebral arteriosclerosis. The severity varied greatly in the fourth to tenth decades and was not correlated with age. Early lesions appeared to be lipid or fatty streaks a few millimeters in length and width, sudanophilic linear deposits, or small oval masses in the intima. The sites of deposition in order of their occurrence were the internal carotid and vertebral arteries, and then the basilar artery and middle cerebral vessels. The anterior cerebral and cerebellar arteries were less frequently and less extensively affected. Of the cerebellar vessels, the posterior inferior cerebellar artery was the earliest and most severely affected. In other vessels, lesions appeared earliest near bifurcations or the ostia of branches. Fibrous plaques appeared in some vessels in patients in all age groups showing lesions. Each of these contained some lipid. Intimal plaques that showed calcification were limited to the internal carotid and vertebral arteries. Hemorrhage was detected in one plaque. In 4 cases, thromboses were superimposed on atherosclerotic plaques. Cerebrovascular lesions (encephalomalacia or hemorrhage) were severe enough to be the cause of death in 12 cases, but not in 5 others. Old, small parenchymal lesions alone were present in 27 patients. Among patients with anatomic evidence of tissue damage from atherosclerosis, the studies in progress on the correlation between the quantitative degree of atherosclerosis in the cerebral and coronary arteries and the aorta of the same patients indicate that aortic lesions are first evident with fatty streaks in the first decade, coronary lesions become evident in the second decade, and cerebral vessel involvement in the third. In each decade, aortic lesions are, on an average, quantitatively greater and coronary artery lesions next, with cerebral vascular involvement appearing to be the least severe.

ANEURYSMS OF THE VERTEBRAL ARTERY. REPORT OF 5 CASES.

Paulson, G.; Nashold, B. S., Jr., and Margolis, G. *Neurology* **9:** 590 (Sept.) 1959.

Aneurysms of the vertebral artery which produce neurologic signs and symptoms are not common, yet they account for 1 to 15 per cent of cerebral aneurysms found at necropsy. One of 5 reported was found at necropsy. The presence of an aneurysm of the veretebral artery was suspected in the other 4 cases and verified by vertebral arteriograms in 2 of them. The symptoms were those of a progressive lesion in the posterior fossa, with signs of intracranial bleeding and headache in the occipital region, which was increased by movement of the neck. All patients except 1 had electrocardiograms indicating myocardial hypertrophy or ischemia, with signs of arteriosclerotic changes in the peripheral vessels. Surgery was performed in 3 patients. In 2, the aneurysms was identified; in 1 of these the aneurysmal sac was opened, and the clot was removed in an attempt to relieve compression on the brain stem, and in the other the veretbral artery was ligated intracranially without reducing the size of the aneurysm. In 1 other patient a syrinx of the cervical cord was aspirated, but the aneurysm was not identified until necropsy was performed. The etiology of the majority of sacular unruptured vertebral aneurysms is not known with certainty but evidence indicates that arteriosclerosis is implicated in most of them. In the 4 cases in this series wherein a necropsy was performed, arteriosclerotic changes were prominent in all vessels including the vertebral arteries. A vertebral aneurysm may have an acute or chronic course. Some patients have no symptoms until the aneurysm ruptures and causes death. Others may have symptoms that vary with the size and location of the lesion. Compression of the adjacent cerebellum, brain stem and cranial nerves, or impairment of the blood supply to these areas, produces neurologic signs. Dull pain in the neck or in the back of the head is a common complaint. Mental changes may include episodes of psychosis or mental confusion. Patients eventually will usually show emotional lability, and generalized seizures are sometimes seen. The fifth and seventh cranial nerves appear to be especially vulnerable. Bilateral sixth nerve palsies may be characteristic of aneurysm in this location. Signs and symptoms of damage to both motor and sensory tracts are present; the patient is partially paralyzed on one side. Weakness is consistently found. A wide-

based gait is usually present. The symptoms of an aneurysm may appear long before death; but in patients with a large saccular aneurysm, intractable nausea and vomiting, debility and loss of weight finally develop. They become bedridden with increasing neurologic deficits. Bulbar paralysis appears. Respiratory failure with pulmonary infection was the terminal event most frequently observed in this series.

PRIMARY HYPERTENSION IN THE ELDERLY.

Perera, G. A. *Ann. Int. Med.* **51:** 537 (Sept.) 1959.

A study was made of the clinical characteristics of 100 patients with documented primary hypertension who were over 60 years of age and who had been under observation because of hypertension at or before the age of 50. Thirty-three were followed until death, and 67 are still living. Long survival and normal life expectancies were observed frequently. The only apparent differentiation from other patients with primary hypertension lay in the fact that minimal elevations of diastolic blood pressure were found in the majority of this group. In the remainder, unusually high casually recorded pressures were the rule, often with marked lability demonstrable with rest. These data suggest that the "floor" of the diastolic blood pressure, if the arterial tension is related to the development of complications, may be more important than the mean or peak values. (From author's summary.)

ANGINA PECTORIS. I. A VARIANT FORM OF ANGINA PECTORIS. PRELIMINARY REPORT.

Prinzmetal, M.; Kennamer, R.; Merliss, R.; Wada, T., and Bor, N. *Am. J. Med.* **27:** 375 (Sept.) 1959.

This form differs from classic angina pectoris in that pain is not produced by increased cardiac work, is usually more severe and of longer duration, may wax and wane in cyclic fashion, is likely to occur at the same time each day, is not relieved by rest, causes greater distress, is not precipitated by emotional stress, and strikes without warning or apparent cause. Should a myocardial infarction occur in the variant form, anginal pain is abolished immediately. Its electrocardiographic features also differ: 1) The ST segments are elevated transiently and often considerably during an attack, but there may be no ST changes in a mild attack or at the onset of a severe attack. 2) Reciprocal ST depression occurs in standard leads. 3) ST and T wave changes during an attack occasionally may seem to improve a previously abnormal electrocardiogram. 4) Areas of myocardium giving rise to ST elevation correspond to the distribution of a large coronary artery. 5) The area of myocardium giving rise to ST segment elevation during anginal pain often is the site of future infarction. 6) Exercise does not produce ST elevation. 7) The R wave may become taller and broader during an attack. Arrhythmias, particularly ventricular, occur much more frequently during an attack of this kind of angina. The variant form is not a rare syndrome, although its incidence is not known. It occurs primarily in persons between the ages of 40 and 60 years and is more common in men than in women. Temporarily increased tonus of a large narrowed coronary artery may be the cause of pain in the variant form of angina. It previously has been shown that the chemical changes in the myocardium differ from those occurring in classic angina pectoris. The variant form may follow a variety of courses. Death can occur during an attack. Progressive coronary artery disease may develop, or the attacks may gradually disappear. The variant form can be diagnosed clinically if a careful history is taken and attention given to the characteristics of the disease. The administration of nitroglycerin distinguishes the variant and classic forms from other cardiac syndromes. If sufficient nitroglycerin is given to cause a mild throbbing headache, the pain in the variant form disappears about one minute after the drug is given and with the onset of headache. If an electrocardiogram is required to confirm the diagnosis, it is essential that two readings be made, one during pain and the other immediately after. Demonstration of the ST segment elevation with its complete disappearance

after a short time identifies the variant type. The administration of nitroglycerin may be life-saving in this kind of angina. Longer acting nitrites may prove helpful in prophylaxis. Observations on a few patients indicate that nylidrin hydrochloride may prevent attacks of this angina. It is given in a dosage of 6 to 12 mg. several times daily. Anticoagulants are indicated for preventing a subsequent infarction. Drugs to combat arrhythmias should be given to patients in whom such attacks occur.

ARTERIAL THROMBOSIS WITHOUT ARTERIOSCLEROSIS AND THE PROBABLE ROLE OF INCREASED PULMONARY MEGOKARYOCYTES IN ITS FORMATION.

Sharnoff, J. G. 32nd Scientific Session, Am. Heart Assoc., October 23–25, 1959, *Circulation* **20:** 769 (Oct.) 1959, Part 2.

A number of instances of coronary, cerebral, and mesenteric artery thrombosis can be shown to have developed in normal arteries free of sclerosis and a possible explanation of their development is suggested. This material lends support to the contention of White that coronary artery thrombosis (or any thrombosis—author) may be produced by two separate factors, namely, arteriosclerosis and an as yet unknown alteration of the blood predisposing it to thrombosis. The concept of the second factor is no doubt derived from the all-too-frequent observation at the autopsy table of severe coronary arteriosclerosis without thrombosis. The observation of thrombosis without arteriosclerosis, though occurring rarely, only adds further emphasis to the possibility that the alteration of the blood alone may lead to arterial thrombosis. It is suggested that the blood alteration which may cause this is produced by the rapid addition of platelets to the blood formed from the break-up of an increased number of pulmonary megakaryocytes. It would appear from recent studies by the author in animals and human beings that stress may cause an increase of megakaryocytes in the pulmonary vessels and that further stress may cause the megakaryocytes to break up rapidly into platelets under the pounding rapid heart action of the right ventricle. Associated with this increase in platelets there is usually blood hypercoagulability. The blood hypercoagulability associated with arteriosclerosis represents the usual combination of factors leading to thrombosis, but blood hypercoagulability alone may also cause thrombosis.

SERIOUS COMPLICATIONS OF PEPTIC ULCER AFTER ACUTE MYOCARDIAL INFARCTION.

Shipp, J. C.; Sidel, V. W.; Donaldson, R. M., Jr., and Gray, S. J. *New England J. Med.* **261:** 222 (July 30) 1959.

Myocardial infarction may be associated with an increased gastric secretory response and activation or appearance of peptic ulcer. Six cases of serious complications of peptic ulcer during the acute phase of myocardial infarction are reported. Perforation occurred in 4, and bleeding in 2. These complications assume added significance and present special problems in management. Emphasis should be on prevention. It is recommended that a patient with acute myocardial infarction together with past or present symptoms suggestive of ulcer, receive an ulcer regimen prophylactically, and that anticoagulants be withheld or used with extreme caution. In 4 of 10 consecutive patients with acute myocardial infarction, uropepsin excretion was elevated. In all 4 it returned to the normal range during convalescence. Of a control group of 10 patients with coronary-artery disease without recent infarction, none had elevated uropepsin excretion. There was no demonstrable difference in the adrenal response in the two groups. It is suggested that, in certain cases, a myocardial infarction may constitute an acute ulcerogenic stimulus. (From authors' summary.)

OPTIC NEURITIS AND UNCONTROLLED DIABETES MELLITUS IN 14 PATIENTS.

Skillern, P. G., and Lockhart, G., III. *Ann. Int. Med.* **51:** 468 (Sept.) 1959.

Fourteen patients with optic neuritis or optic atrophy and uncontrolled diabetes mellitus were selected for study; patients with any condition known to cause optic neuritis

other than diabetes mellitus were excluded. Three patients in the series used tobacco; 2 patients drank alcohol. The ages ranged from 40 to 69 years. All patients had noted loss of vision. Examination disclosed that 12 patients had undiagnosed moderate or severe diabetes mellitus. Blood sugar values on admission were more than 200 mg. per 100 ml. in all patients except 1; in 7 they were more than 300 mg. per 100 ml. Thirteen patients had 3 or 4 plus glycosuria. Nine had symptoms of diabetes mellitus. Three had peripheral diabetic neuritis. Diabetic acidosis was absent in all of the patients. The onset of the visual loss was gradual in 16 eyes and rapid in 6 eyes. The visual loss, ranging from moderate to severe, was bilateral in 8 patients and unilateral in 6 patients. Papillitis was observed in 7 eyes and optic atrophy in 13 eyes. Seven eyes had central scotomata, and 11 had peripheral contraction of the visual fields. Control of the diabetes mellitus arrested the visual loss in all but 1 of the patients who were followed. However, only 1 patient showed significant improvement in vision after the diabetes mellitus was controlled. On the basis of data gathered from several previously published case reports and the 14 patients in this series, it is suggested that visual loss may be caused by the toxic effect of uncontrolled diabetes mellitus on the optic nerves in susceptible patients. (From authors' summary.)

MANAGEMENT OF THROMBOPHLEBITIS WITH PHENYLBUTAZONE.

Stein, I. D. *Am. J. Cardiol.* **4:** 476 (Oct.) 1959.

That phenylbutazone is an effective treatment for superficial thrombophlebitis is demonstrated by the 97 per cent complete resolution among 706 cases of various types when treated with this drug. This was accomplished by administering 30 tablets (3 Gm.) in the course of a week or less. The patient can be treated at home or in the office. The rapid improvement also spares the patient financial loss because he is able to return to work as soon as the pain subsides, that is, in a matter of days. The use of phenylbutazone has been extended successfully to the treatment of phlebitis of the deep veins. Among 79 such patients, 59 had been hospitalized and given anticoagulant drugs before receiving phenylbutazone. When phenylbutazone was given because of progression of the phlebitis or lack of clinical improvement, pain and discomfort lessened within twelve to twenty-four hours, body temperature fell, and swelling softened and diminished. Walking could be resumed and the hospital stay was shortened to an average of five to seven days. Mechanical blockage of the large venous channels manifested by the peripheral edema noted when the patient has been on his feet, could be controlled by elastic compression. It is recommended that anticoagulants be given in conjunction with phenylbutazone in recent cases of thrombophlebitis of deep veins. No serious complications occurred in the treatment of 785 patients. Short-term therapy may in part have accounted for this absence. The minor reversible side-effects were dyspepsia and heartburn (5 per cent of patients), skin eruptions (0.5 per cent), and generalized edema (0.5 per cent).

THE WEIGHTS OF BRAIN, HEART, SPLEEN, LIVER, AND KIDNEYS IN MENTALLY SICK PATIENTS DYING IN THE AGE FROM 60–95 YEARS. THEIR RELATION TO SEX, NUTRITION, PSYCHOSIS, AGE, AND FATAL DISEASE.

Strassmann, G. *Proc. IV Congr. Internat. Assoc. Gerontology* (Merano, Italy, July 1957), Vol. II, Clin. Div., p. 423; through Excerpta Med. (Gerontol. & Geriatrics) **2:** 254, 1959.

In elderly mentally sick patients there is a tendency towards decrease of weight and atrophy of parenchymatous organs, especially the spleen and liver. This atrophy is frequently associated with general malnutrition and emaciation of the body. Many of these patients are feeding problems. Often atrophy develops independently from the nutritional state of the body; atrophy of the spleen, liver and kidneys was observed in obese patients dying at ages from 60 to 95 years. The weight of the brain depends on many factors and did not correspond in many instances to the general nutrition of the body. One of the most

important factors for the weight is the amount of blood present at the time of death, depending on the type of death and fatal disease. Another factor is the amount of tissue fluids in the substance of the organs, and in the brain in the ventricles and subarachnoid space. Elderly emaciated patients of both sexes sometimes had brains weighing 1,500 Gm., and obese patients had atrophic brains with a weight of 1,000 Gm. or less. The average weights and the minimal weights of all organs were lower in the females than in the males. Atrophy of the heart was generally associated with severe emaciation of the body, and hypertrophy of the heart with obesity. The average weight of the heart was higher than in normal adults, due to the effects of atherosclerosis of the heart valves, coronaries and aorta, hypertension, and nephrosclerosis. Many factors account for the weight of the organs. In elderly mentally ill patients a tendency exists towards a decrease in the weight of the brain, spleen, liver, kidneys and often also of the heart. The causes of the atrophy are partially due to disturbances of the blood supply, its impairment and resulting ischemia, infarctions and scars, and partially to loss of substance and tissue elements without conspicuous circulatory disturbances, as a process of aging. Shrinkage of organs is not always in correspondence with malnutrition; it can also be associated with obesity. The reasons for such atrophy in the patients of the higher age groups are of a complex nature and not yet fully understood.

THE CLINICAL IMPLICATIONS OF HYPOGAMMAGLOBULINEMIA IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA AND LYMPHOCYTIC LYMPHOSARCOMA.

Ultmann, J. E.; Fish, W.; Osserman, E., and Gellhorn, A. *Ann. Int. Med.* **51:** 501 (Sept.) 1959.

The records of 33 patients with chronic lymphocytic leukemia (CLL) and of 27 with lymphocytic lymphosarcoma (LL) were analyzed. The age range was from 23 to 82 years; half of the patients were past age 50. Hypogammaglobulinemia (HGG) was found in 19 (30 per cent). Among these, twice as many patients (13) had CLL as LL (6). The low gamma globulin levels usually were observed late in the course of the disease. They often, but not invariably, occurred in patients with extensive involvement by disease, so that no conclusion could be drawn as to a direct relation between the extent of lymphoid involvement and the appearance of HGG. HGG modified the course of each of the disease processes, the patients becoming subject to recurrent infection, particularly with *S. aureus*. Infection occurred in 89 per cent of the patients with HGG but in only 15 per cent of those without low gamma globulin levels. The staphylococci cultured almost always proved resistant to the antibiotics commonly in use. However, infections usually improved with the use of local measures, the administration of various antibiotics, or the administration of gamma globulin. The gamma globulin level increased in only 1 of the 19 patients during general hematologic improvement. It did not, however, reach normal levels in this patient with a steroid-induced remission. The gamma globulin level fell progressively in 13 (despite general and hematologic improvement in 7 patients), remained static in 2 patients whose disease was also static, and remained unchanged in 3 patients although their disease progressed.

SOME UNUSUAL MANIFESTATIONS OF CEREBRAL ANEURYSMS.

Werman, R.; Christoff, N., and Bender, M. B. *Am. J. Cardiol.* **4:** 452 (Oct.) 1959.

Case reports are given for 6 patients with cerebral aneurysms that presented difficulties in diagnosis. Cardiovascular conditions that might have been the cause of the cerebral condition were present in 4 patients, hypertension being the most frequent misleading symptom. Vasculitis was present in 2 patients, but it was later found to bear no relation to the aneurysm. When a patient with acute pulmonary edema and concurrent coma be-

came psychotic, this change was thought to be a manifestation of cerebral circulatory insufficiency secondary to congestive heart failure. Blood discovered in the subarachnoid space led to the belief that a clotting defect had occurred due to the administration of dicumarol. Meningeal signs continued absent in 2 cases with subarachnoid bleeding; 1 patient with mild meningeal signs had an acellular spinal fluid. Traumatic spinal puncture rather than intracranial bleeding was assumed to be the cause of bloody spinal fluid in another patient. Constant red cell counts in multiple tubes, xanthochromia of the supernate, and failure of blood to coagulate suggest a nontraumatic origin for the blood. As for symptomatology, marked personality changes occurred in 3 patients. Aphasia was a major symptom in 2 patients, one of whom also exhibited right focal seizures and left optic neuropathy. Unusual location of the aneurysm accounted for unusual symptoms in 2 cases; in one, the patient had severe facial pain and unilateral ophthalmoplegia from an infraclinoid aneurysm involving the trigeminal nerve in the area of the gasserian ganglion. The other had an aneurysm of the posterior circulation, the symptoms of which were thought to be caused by multiple vascular episodes. Posterior circulation locations account for approximately one quarter of cerebral aneurysms. Two separate episodes with different symptoms occurred at widely spaced intervals in 3 cases. The initial symptoms in these cases were headache, or headache and coma thought to be a "stroke," and internal rectus palsy thought to be related to a local eye disorder. Incomplete arteriography was a diagnostic pitfall in 3 cases. The diagnostic difficulties in such instances can be overcome by awareness of the possibility of cerebral aneurysm in cases of cerebral disorders, a knowledge of the various modes of presentation, the knowledge that an aneurysm is always the most likely cause of cerebral bleeding in the absence of an unmistakable explanation such as severe cranial trauma, and performance of lumbar puncture and complete angiography in most cases.

BOOKS RECEIVED

Receipt of the following books for review is hereby acknowledged. We are glad to publish complete listings of all new books received but such listing must be regarded as a sufficient return for the courtesy of the sender. Books of particular interest will be reviewed in full as time and space permit. Additional information in regard to all listed books will be gladly furnished upon request.

CARCINOGENESIS BY ULTRAVIOLET LIGHT. An Assay in Quantitative Biology. By *Harold F. Blum*. Dr. Blum is Physiologist with the National Cancer Institute, National Institutes of Health, U. S. Public Health Service, and is presently Visiting Professor of Biology at Princeton University. Cloth. $6.50. Pp. 340. Princeton University Press, Princeton, New Jersey, 1959.

THE PROCESS OF AGING IN THE NERVOUS SYSTEM. Thirty-Two Contributors. Edited by *James E. Birren, Ph.D., Henry A. Imus, Ph.D.* and *William F. Windle, Ph.D., Sc.D.*, U. S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, Bethesda, Maryland. Cloth. $7.00. Pp. 224. Charles C Thomas, Publisher, Springfield, Illinois, 1959.

THE ARTERIAL WALL. Edited by *Albert I. Lansing, A.B., Ph.D.*, Chairman, Department of Anatomy, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania. Sponsored by The Gerontological Society, Inc. Cloth. $7.50. Pp. 259. The Williams & Wilkins Company, Baltimore, Maryland, 1959.

RECENT ADVANCES IN CARDIOLOGY. By *Terence East, M.A., D.M., F.R.C.P.*, Physician, and Physician-in-charge of Cardiological Department, King's College Hospital, and *Curtis Bain, M.C., D.M., F.R.C.P.*, Consulting Physician, Harrogate General Hospital. Fifth Edition. 133 Illustrations. Cloth. $10.00. Pp. 421. J. & A. Churchill Ltd., London, and Little, Brown and Company, Boston, Massachusetts, 1959.

A NEW LIFE IN YOUR LATER YEARS. By *Dr. Heinz Woltereck*. Translated by Charlotte Haldane. Dr. Woltereck, an eminent biologist and psychologist, studied at Freiburg-Greisgau, Munich and Leipzig Universities. He has achieved a notable place in Europe as the author of a number of books on scientific subjects. "A New Life in Your Later Years" is his first book to be translated into English. Cloth. $3.75. Pp. 194. The Dial Press, Inc., 461 Fourth Avenue, New York 16, N. Y., 1959.

MEDICAL DISCOVERIES: WHO and WHEN. By *J. E. Schmidt, Ph.B.S., M.D., Litt.D.*, President, The American Society of Grammatolators; Chairman, National Association on Standard Medical Vocabulary. Cloth. $14.75. Pp. 555. Charles C Thomas, Publisher, Springfield, Illinois, 1959.

Ciba Foundation Study Group No. 1. PAIN AND ITCH: Nervous Mechanisms. Edited by *G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P.* and *Maeve O'Connor, B.A.* Cloth. Pp. 120. 41 Illustrations. Little, Brown and Company, Boston, Massachusetts, 1959.

Ciba Foundation Study Group No. 2. STERIC COURSE OF MICROBIOLOGICAL REACTIONS. Edited by *G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P.* and

Cecelia M. O'Connor, B.Sc. Cloth. Pp. 115. 37 Illustrations. Little, Brown and Company, Boston, Massachusetts, 1959.

The Ciba Collection of Medical Illustrations. Volume 3. DIGESTIVE SYSTEM. Part 1. *Upper Digestive Tract.* Prepared by *Frank H. Netter, M.D.* Edited by *Ernst Oppenheimer, M.D.* Cloth. $12.50. Pp. 206. In the United States, copies may be obtained from the Publications Department, CIBA Pharmaceutical Products Inc., Summit, New Jersey; in other countries, inquiries should be directed to the nearest CIBA office.

PLANNING HOMES FOR THE AGED. Edited by *Geneva Mathiasen*, Executive Secretary, National Committee on the Aging, National Social Welfare Assembly and *Edward H. Noakes*, Edward H. Noakes & Associates, Architects. Cloth. $12.75. Pp. 119 (8½″ x 11¼″ size). F. W. Dodge Corporation, 119 West 40th Street, New York 18, N. Y.

HUMAN NUTRITION AND DIETETICS. By *Sir Stanley Davidson, B.A.Cantab., M.D., F.R.C.P.Ed., F.R.C.P.Lond., M.D.Oslo*, Physician to Her Majesty the Queen in Scotland; Regius Professor of Medicine, University of Aberdeen, 1930–1938; Professor of Medicine and Clinical Medicine, University of Edinburgh, 1938–1959; Physician-in-Charge, Royal Infirmary, Edinburgh, 1938–1959; *A. P. Meiklejohn, M.A., B.Sc., D.M.Oxon, M.R.C.P. Lond.*, Lecturer in Nutrition, University of Edinburgh; Formerly Instructor in Medicine and Francis Weld Peabody Fellow, Harvard University; Consultant in Nutrition, European Regional Office, United Nations Relief and Rehabilitation Administration; and *R. Passmore, M.A., D.M.Oxon.*, Reader in Physiology, University of Edinburgh; Formerly Lieutenant-Colonel, Indian Medical Service. Cloth. $15.00. Pp. 844. E. & S. Livingstone Ltd., London. The Williams and Wilkins Company, Baltimore, Maryland, exclusive U. S. agents, 1959.

Books for review should be sent to Edward Henderson, M.D., Editor-in-Chief, 236 Midland Avenue, Montclair, New Jersey.